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MEDICAL INTERLUDE*

Some Observations on English Medicine with Further Reflections on "the Consolations of Medicine."

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"The skill of the physician shall lift up his head."—Ecclesiasticus.

It so happened that this past summer the writer was able to enjoy an experience which every practising physician requires at not too long intervals—to play the observer and watch the drama of medicine from the stalls. Such an experience probably has some value in the practical knowledge which one may gain from seeing how the other fellow is playing his part but it undoubtedly has greater value in enabling one to see his profession in perspective and to do a little reflecting about things in general and medicine in particular.

British Clinical Medicine.

Most of my time was spent in the wards of the London hospitals where tradition and the most recent discoveries in medical technique are constantly jostling one another. I was impressed by three things in British clinical medicine. The first, the emphasis which is placed upon clinical observation, the insistence at all times upon the prime importance of the physical examination and of the findings gained from the use of the physician's five senses and his sixth or clinical sense. The laboratory is always an auxiliary aid. This is not to belittle the rôle of the laboratory but to assert the tradition and common-sense methods of Sydenham which have been the particular contribution of the English genius and character in medicine.

Closely related to this clinical approach is the second observation—the English attitude towards the patient. This has never been expressed better than in the principle which was laid down by Osler, "that the patient who has the disease is as important as the disease that the patient has." There is profound English humour in those words and not a little of the wisdom that humour always conveys. Sir Clifford Allbutt stated the same idea in other semi-ironical words—"Life is dear, even to a layman." This insistence upon the individuality of the patient is a cardinal characteristic of the English method in medical training and practice. It is clinical wisdom of the most practical kind. In the pressure and routine of practice we physicians are always apt to forget that we cannot classify patients in our conventional pigeon-holes of nosology. In the last analysis every illness is a simple or complex factor multiplied by a second factor that is always complex—the individual who is suffering from the disease. The result must always be that the illness is a special problem demanding a special solution. Hence the physician must see general divisions of the disease resolving into particular cases.

And the third observation is the ability of the physicians of the Old Land by their breadth of learning and by their humanity to relate medicine to the general life of mankind, their ability to reconcile the talents of the highly trained efficient physician with the attributes of a man of culture. This achievement which seems to be a matter of natural growth rouses envy and despair in the mind of the man whose life has been lived in the restless prac-

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Editor's Note.—Dr. E. P. Scarlett was the original Editor and Founder of this Journal and thereby gained the distinction of editing the first Undergraduate Medical Journal on this continent. We welcome his return to these pages.

tical world of this continent with its emphasis on utilitarian values. How is it done? On what sources does it rely? I for one have no answer to those questions. An answer involves matters which lie beyond the field of medicine and involve the whole manner of life.

Medical Confessions.

In the foregoing remarks I have set down some observations of a professional nature But I said at the outset that not only does a physician when he is foot-loose visit clinic and hospital, but with the little leisure which modern travel brings him he is apt to think about his profession as a whole. Depending on the mood at the time, his reflections may be gay or serious or profane. For some reason or another in recent years the medical profession, always a model of reticence, has become as fond of self-revelation as any group of prima donnas. Only recently the shrewd, hard-bitten Kansan, Dr. Hertzler, has proclaimed himself to the world in 'The Horse and Buggy Doctor.' For him the reward of medicine is in the daily round of tasks. But he is quite sure that if the world were rid of clergymen and lawyers and neurotic women, the practice of medicine would be incomparably improved. "If ministers would just forget the hell hereafter and concentrate on the hell on this earth, if lawyers would forget the law and concentrate on justice," and if the neurotic lady would "marry a profligate and drunken husband," the doctor's job would be so much easier. Such is only one of the strains in the medical refrain which is entertaining an eager public at the moment.

Any reflections along this line which I may have made this summer in moments of leisure were less particular and under the circumstances more sober. They were the thoughts that any physician would have as he walked about the decks of his ship on the high seas, half-way between two worlds, leaving behind him the dark and troubled atmosphere of the old world and sailing towards the new world with its social and economic unrest. What of his craft of medicine in such a setting? Not so much what its future would be in the scheme of things, nor whether eventually it would come under the governing eye of the state but rather what satisfaction did it offer to one who found himself in its ranks in the troubled world of to-day? Consciously or unconsciously that is a question which every student preparing himself for the practice of medicine and every physician must ask himself on some occasion. It was the question which came into my mind this summer, and I found myself thinking of medicine in terms of the rewards which it has to offer. Then I remembered that over thirteen hundred years ago in a similar time of unrest and political storm the old philosopher Beothius wrote his "Consolations of Philosophy" (and in prison at that). I began to wonder what the "consolations of medicine" might be to a physician of to-day, and so, in the way of an embryo philosopher, I gradually proceeded from the particular to the general.

The Consolations of Medicine.

Now at some time or other every one in the profession has listened with the deep understanding of a fellow of the craft to the angry outbursts of a harassed physician after he has made a call upon a particularly querulous patient. We have all seen a physician at the end of a long day's round when he casts off the professional mask and becomes a modern Ecclesiastes, or when, echoing old Solomon, he cries out, "Comfort me with apples and stay me with flagons, for I am sick of practice!" Assuredly an essay is still to be written on the woes of the doctor—the work under pressure, the unreasoning demands of patients, the lay public's demand for "penny-in-the-slot" diagnosis and an absolute cure, the inability to prescribe what so many sufferers need—money.

The span of the physician's life might be written in three phases (if we choose to be Olympian in our view). The first period comprises the ten years of training in college, medical school, and hospital. There follows the second stage—the early years of practice while he is becoming what is popularly known as established, eking out a small living, doing unpaid work in clinics and hospitals, above all never appearing to be unsuccessful, and, through it all, if he is to remain vital, virtually consuming his stores of youthful idealism against the day of his success. At forty or shortly after, he passes into the third period, achieving his professional success, is caught up in the whirlwind of activity in practice and medical organizations, takes his place in those activities in public life expected of him, educates his family with whom he endeavors to become acquainted in short summer vacations; whirled in the maelstrom of modern life, he struggles to keep up with the increasing tempo of medical practice, is invariably late for appointments, snatches a little vicarious pleasure in occasional sport, and in odd moments of contemplation smiles wryly at the words of Osler, the medical prophet of a more leisurely generation, whose counsel to the physicians was "aequanimitas," a calm spirit, but whose master-word was "work." And finally, as often as not, while he is still bewildered, or in a mood of frustration, or meditating retirement, there comes an early death (the average age of death of physicians, according to figures, being sixty).

It is little wonder, then, that at times there are outbursts against the tyranny of it all.

There are those who will protest that in sketching the three acts of a physician's life in this manner the harsher lines are over-stressed and the shadows exaggerated. Life after all, they point out, is never a perfect business, more especially to the tired eyes of a physician. As a man unwinds the thread of his hopes and fears there are experiences and satisfying pleasures that outweigh the weariness, the fever and the fret of the difficult moments. We are told that no calling is richer in these consolations than medicine, and in the past these abiding rewards of medical practice have been set forth in an aura of over-sentimentality. But it is a fact worth pondering that even to-day, when a sense of sterner realism prevails and when many people think of a physician as a hurried, business-like man in white coat who charges large sums for ambiguous advice, there is still an appreciation of the essential values of medical practice. A mood of disenchantment may prevail with regard to the world at large, but medicine still remains firmly rooted, nourished by a regard for the ancient mystery of healing.

What are the consolations of medical practice? Before answering the question, one should set down the immediate stimuli under which a physician carries out his work. Each practitioner doubtless has his own, but there are some that may be regarded as common to all. First, and necessarily so, there are the great social drives of subsistence, family life and material success —the necessity of "earning the damned guinea," as John Hunter called it. Then the insistent call to work—nowhere more evident than in medicine—which plucks even the most tardy by the hair. There are the constant urge and example of the tradition of healing, the unwritten laws of practice which must be obeyed. And, not the least, there are the intrinsic interest of the work and the fascination of the game, making demands of the hand and the mind.

These factors, of course, are common to most vocations and in the calling of medicine as elsewhere may carry within themselves their own reward. Certainly it is something to have learned—even under compulsion—a sense of the value and virtue of work. The physician may thank the gods that his education has been salted by the winds

of action. He has learned with Leonardo da Vinci, that supreme craftsman, that all things good have been given to man at the cost of labour. The traditions of medical practice under which he constantly works give him a sense of discipline, that power to meet with cheerfulness and resource what Kipling calls "the minor damnabilities of life." And with discipline usually is acquired the courage which sustains him in those times when he must eat his bread in sorrow and bitterness. However exacting at times may be the traditions of practice, it remains that for every physician the constant guide in the day's work is loyalty to the traditions and standards of his profession, in the same way that for Scotsmen the world over, the porridge and the heather and the Psalms of David last to the third generation as a sustenance for mind and body. And if the secret of success in life is the amassing of loyalties, medicine in this particular becomes a worthy, light and honourable bondage.

But what of the larger consolations peculiar to medicine that may solace the tired, disillusioned physician? They are more difficult of statement, less obvious and are for the most part implied in the relation of physician and patient. They may be dimly traced when in an hour of relaxation the physician turns over such matters in his mind. One need not be sentimental nor hardly assertive of the time-worn aphorisms of a medical graduation address to consider some of them.

It may be said at once that the physician who carries through his practice conscientiously is a philosopher without knowing it. He is supported by great forces which are operating through and about him in his work and if at times he thinks about what he is doing and about the relation of his work and his profession to the world at large, he will at once be aware of certain privileges which are his.

The present state of the world is one of confusion, disorder and social unrest. To use a medical tag, it is a paranoid world. In this environment the individual mind is anxious and disquieted. One thing that helps to keep the world on its feet is the assured advance of science in the midst of superstitions and passions. Medicine with its applied science is a stabilizing force of the greatest importance and the physician able to work constructively within this atmosphere is enjoying a privilege that is inestimable, at a time particularly when so many contemporary activities seem sterile.

At a time too when humanity is on the march and being continually disturbed by bold speculations and strange gospels, the physician is fortified by his knowledge from training and experience that emotion, to be of any value, must have a strong skeleton of intellectual principles. No one should know this better than the physician. And at the same time his calling, in its intimate contact with nature and mankind, should enable him to perceive the essential irony of life—corporate and individual, its glory and its futility. If he translates this irony into a philosophy of agnosticism, he is saved from its excesses and from a hardening of outlook by the reality of daily practice. As Clifford Allbutt pointed out, the practice of medicine safeguards a man against the withering sin of cynicism; no good physician was ever a misanthrope.

But whatever philosophy of life he may have acquired, the practitioner has the supreme advantage of being able, of being forced to remain in the arena and act. He is not allowed by his calling to remain the ineffectual philosopher, he cannot play the Hamlet and survive. His body is balanced and corrected by the operative values of things and by action. It is noteworthy that in his most recent novel, Aldous Huxley, in discussing the dilemma of the intellectual man of to-day, puts his doctrine of freedom into the mouth of a physician. Freedom for the skeptical intellectual, he asserts, consists not in

detachment but in identifying himself with other human beings.

Medical training then gives the physician a philosophy; it is balanced and tempered by the activity of practice. And in his work the practitioner learns other things that breed a wide tolerance and a great sympathy. He soon finds that disease is much more than a matter of bacteria. Younger people are harassed by work and worry; elders are trying to ward off the forerunners of decay. He realizes with Amiel that "everyone is imprisoned; everyone has his tic, his limitations, his mental deformity; his vision is good in the things of his own province, but his competence is narrow." With this understanding the medical man still has it within his power, through the scientific method of approach and through the art of medicine, to work actively within these limits, to discern and utilize values, and to labour for concrete and enduring achievements. Thus he is emancipated from the great "pathetic fallacy" of our time—false sentiment about human nature and life which is sterilizing our modern humanitarian movements, and from the superstition of greatness and sensationalism that is destroying so much of the modern sense of values.

Through it all it is his part as a physician to give people confidence, to supplement by some mystical spiritual reinforcement which their bodies claim from science that invincible courage which is the most miraculous attribute of human nature. It is at this point that the small sphere of scientific medicine ends, and the larger, age-old healing ministry of medicine in its highest form begins.

Nor does the physician travel alone. The whole army of medical science is with him. He faces life not as a beggar but proudly bearing gifts. He is constantly heartened by new medical discoveries which are, in Harvey's quaint phrase, being steadily drawn up from the well of Democritus. With sagacity gained from working with human nature, manual dexterity, the quiet reserve of a truly ironical spirit, a kind heart and a conscience, the hosts of a depressed world shall not prevail against him.

At the outset we somewhat harshly divided a physician's life into three acts. We still stand by that outline, but whatever was pessimistic in that portrayal has been resolved on closer examination. The life of a physician has been seen to be compacted of some of those ingredients which wise men have claimed for a rich life. During the first period of training in college there are the rewards of the scholar who "scorns delights and lives laborious days," the rewards of Browning's Grammarian who would "not discount life." During the early lean years of practice he experiences the blessings of the self-denying ordinance of the monastic orders—brothers in poverty. And in his maturity, in the full tide of practice, he has the supreme satisfaction of the joy of living, of touching life at all points; in the familiar tag he experiences "one crowded hour of glorious life," and if the hounds are in close pursuit, so much greater the satisfaction in keeping up the chase. When finally there comes the swift end when he is still at the height of his power and activity, what better salute for one who has not loved life but living than to go out without complaint. As Stevenson says, "Does not life go down with better grace, foaming in full body over a precipice, than miserably straggling to an end in sandy deltas?" His words might be a doctor's creed.

If from all this moralizing the physician can gain but scant consolation, it is still possible that the very circumstances of his daily round of work may yield at the last their own reward. Sir Andrew Macphail in his memoir of John McCrae, quotes these words of McCrae to his students:

> "It will be in your power every day to store up for yourselves treasures that will come back to you in the consciousness of duty well done,

of kind acts performed, things that having given away freely you yet possess. It has often seemed to me that when in the Judgment those surprised faces look up and say, 'Lord, when saw we Thee anhungered and fed Thee; or thirsty and gave Thee drink; a stranger and took Thee in; naked and clothed Thee'; and there meets them that warrant-royal of all charity, 'Inasmuch as Ye did it unto one of the least of these, Ye have done it unto me,' there will be amongst those awed ones many a practitioner of medicine."

These consolations of medicine, fragmentary and arbitrary, are neither comprehensive nor absolute, but they represent a few of those things most sovereign in a world that has again fallen to the ancient rulers of fear, pride, cruelty and intolerance.

THE TREATMENT OF GONORRHOEA

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It is indeed a privilege to be given the opportunity of contributing an article to the University of Toronto Medical Journal.

I make no apologies for my subject, for although this disease dates back to the very dawn of history, one is forced to believe that all too little is known of the technique of treatment by many modern physicians, if one must judge from the innumerable bungles which come to one's attention. Also, I wish to state here, that I will be relating no new or original forms of treatment, but only reiterating principles and details now well recognized and often written about, but certainly, too often neglected, chiefly on account of lack of interest on the part of the physician, when the sufferer presents himself for advice. Surely it is truly lack of interest when, on being consulted by one suffering from a urethral discharge, a doctor does not trouble even to examine the external genitalia, nor to examine a smear from the discharge or observe the characteristics of a specimen of urine. "Omission" of careful examination is more frequently the cause of poor end results of treatment than is "Commission" of errors in that treatment. With the hope that this short message may reach the eye of many soon to step over the threshold into the role of general practitioner, I present the following on the treatment of gonorrhoea. My remarks will be confined to the treatment of acute gonorrhoea in the male, since to enter into the details of treatment of chronic gonorrhoea, and its numerous complications as well as gonorrhoea in women and children, would necessitate an article much more extensive than I will attempt at the present time.

General Instruction to All Cases

Certain general information should be given the patient, no matter in which stage of the disease he presents himself. He should be told that he is suffering from a contagious disease which he may carelessly spread to others or which, by neglect of treatment or thoughtless habits, can be encouraged to spread to deep or distant structures and may even cause such serious end results as blindness by the onset of gonorrhoeal ophthalmia, implanted by the patient's own dirty, infected fingers, or death from gonorrhoeal endocarditis by spread of the infection through the blood stream. Abundance of rest, both of mind and body are important,

sexual stimulation and the use of alcoholic beverages or other irritating articles of food or drink must be avoided. Regular washing of both the genitalia and the hands, particularly after urinating, is desirable. The clothing should be protected from the discharge by wearing a porous gauze penis bag (not a rubberized bag) and no dressing should be allowed over the urinary meatus which could prevent free flow of the discharge from the urethra. The patient should be urged to drink freely of water, milk or buttermilk, during the day, but this quantity should be curtailed during the evening in order that the very necessary period of sleep may not be too frequently interrupted by the act of urination.

Treatment of Acute Gonorrhoea in the Adult Male

This varies according to the stage of the disease at which the patient presents himself. It is customary to speak of the First Stage, the Second Stage and the Third Stage.

THE FIRST STAGE

The First Stage lasts from the very earliest symptom, which is usually slight tickling at the point of the penis and scanty mucoid discharge, for about eighteen to twenty hours. During this time, the organisms are said to be mainly on the surface of the urethral mucosa and stained smears of the discharge show pus cells and a preponderance of extracellular diplococci. May I say here, that the presence of a urethral discharge, is not, in itself, sufficient evidence on which to make a positive diagnosis of gonorrhoea and the examination of smears must never be neglected, and culture should be done, if a diagnosis entirely beyond criticism is required.

During this stage, treatment may be of an abortive nature. Previous to the advent of sulphanilamide therapy there were three methods available for use in this early and mild condition. One may prescribe— (1) Hand injections, to be carried out by the patient, using preferably an inorganic silver preparation such as argyrol 10% or protargol ½% every three hours for three days.

(2) Irrigations, to be performed either by the physician or by the patient following careful instruction by the physician, and using potassium permanganate 1/8000 at 105 to 110 degrees at very little pressure.

(3) The Ballinger "Sealed-in-Treatment" which must be done by the physician.

Since the sulphanilamide treatment as well as the use of injections and irrigation are of value in all stages of the disease, I will go over details of their use later in this paper, but the Ballinger 'sealed-in' treatment is only useful in this early first stage of the disease and therefore, I will explain its technique here.

THE BALLINGER 'SEALED-IN' TREATMENT OF GONORRHOEA

This treatment must be instituted before there is a definite purulent discharge or a turbid urine, and it must be carried through for at least five days, unless the discharge becomes definitely more profuse or the urine becomes cloudy, when it must be discontinued forthwith. A seal should be applied once in twenty-four hours, it should remain in place about six hours and should be re-applied at once, if it fails to hold for approximately that length of time. A 5% solution of Argyrol prepared fresh each day, is the solution used, and 25 minims are injected and retained in the anterior urethra, by the use of a seal, of *non-flexible collodion* applied by means of a camel's hair brush, over the meatus.

The patient having urinated, the argyrol is injected and held in the urethra by a urethral clamp, or by pressure on the urethra behind the glans, by means of a pair of wooden tongue depressors, the ends of which are compressed by rubber bands. The meatus and glans penis are cleaned with acetone

or ether and thoroughly dried by fanning. The lips of the meatus are then held apart and one layer of the collodion applied. Immediately the meatus is compressed and several further layers of collodion applied, each layer being allowed to dry thoroughly before a second is brushed on. After a reasonably firm cap is built up over the meatus, a reinforcing strip of gauze is anchored down on one side and firmly drawn across the meatus and anchored down on the opposite side. The whole is then given a final application of collodion and thoroughly dried. I have found the drying process hastened by the use of an electric fan. Soiling of the clothing is prevented, when the seal is in place, by covering the penis with a rubber condom.

The seal should remain in place until the patient is compelled to urinate and then it should be carefully removed by soaking with ether or acetone, being particular that the superficial tissues are not injured by attempting to pull the collodion away. Until two hours before the next seal, the patient should drink freely of liquids in order that the urethra be frequently washed free of discharge by urinating. This treatment, although somewhat tedious in performance is highly successful, if carefully carried out on properly selected cases.

I might mention that in a few patients, a chemical urethritis may follow the use of seals and cause a slight discharge which, however, is entirely free of gonococci and clears up in a few days after the seals are discontinued.

THE SECOND STAGE

The Second Stage varies greatly in duration but it is usual to consider it as lasting from the completion of the "First Stage" until definite evidence of the spread of the infection to the posterior urethra is manifested. More or less marked signs and symptoms of an acute inflammation are present, smears show chiefly intracellular diplococci and the urine is hazy to turbid in the first glass and clear in the second. During this stage the gonococci have penetrated between the columnar cells of the epithelial lining and therefore, are more inaccessable to locally applied antiseptics, and treatment should be gentle in character, symptomatic in nature, and it will of necessity be more or less prolonged. It matters not whether treatment is given as irrigations or injections, it matters little what antiseptic solution is used, but gentleness is imperative and if the urethritis is very acute all local treatment should be withheld for a day or two until rest in bed, together with hot sitz baths or external heat applied in other ways has so reduced the acute inflammation that local treatment can be carried out in comfort.

The patient must void immediately before any application is made to the anterior urethra in order that gross pus be washed off the mucous membrane and then either of the following may be done:

1. Irrigation by 1-8000 potassium permanganate solution at 105 degrees, using one or two quarts of solution at a pressure head of one to three feet, once daily.

2. Injection of netural acriflavine 1-2000, argyrol 10%, protargol ½%, neo-silvol 10% using about half an ounce of the chosen solution injected by means of a hand syringe several times daily.

Occasionally both methods may be used on a patient at the same time. Such treatment may have to be persisted in for two or three months.

THE THIRD STAGE

The Third Stage may begin at any time during the course of acute gonorrhoea, it occurs in about 60% of all cases and it is during this stage that one fears the spread of infection to prostate, seminal vesicles, vas deferens or epididymis.

It is not uncommon at the onset of this stage for the urethral discharge to become much less profuse or indeed to disappear completely. but the

general feeling of prostration, the onset of fever, frequency, urgency, dysuria or haematuria and the demonstration of a turbid urine in both first and second glasses will warn the physician that the disease is rapidly overcoming the patient's resistance and gaining a deeper and deeper hold on its victim.

One's skill may be taxed to the uttermost in dealing with this stage but again I would wish to stress the need of gentle and conservative measures rather than too active local treatment which may readily aggravate the inflammation. If the inflammation is very acute or the symptoms severe, the patient should be kept in bed, given abundance of fluids, a rectal suppository of belladonna and opium administered, and a sedative alkaline mixture prescribed. Hot sitz baths several times a day, together with heat to the perineum are always comforting and helpful. When the severe symptoms have abated, local treatment may be instituted following the suggestions outlined above for the "Second Stage." It must be borne in mind, however, that hand injections by the patient will only suffice during the first week or so of treatment and it is usually better to get the patient accustomed as soon as possible to irrigations into the bladder, or to instillations in order that some treatment may thus be applied to the posterior urethra. It is usually folly to carry out any instrumentation or prostatic massage until the patient has been under treatment for three weeks or longer. Should retention of urine occur due to reflex spasm of the sphincter muscle or to the swollen prostrate, catheterization should be done only as a last resort, when a thorough attempt after a hypodermic injection of morphine (without atropine) followed by a hot bath, has not enabled the patient to void.

The treatment of the numerous complications which may arise during this stage cannot be given in detail but I will pass over them rapidly.

1. *Acute Prostatitis* always occurs in this stage but may be very slight. It may resolve completely, it may go on to abscess formation or it may become a chronic condition. A mild inflammation will usually clear up with daily bladder irrigations and gentle massage of the gland. An abscess if on the urethral side of the gland will rupture spontaneously into the urethra, if, however the abscess is deep in the body of the prostate or close to the rectal mucosa it should be opened through a small perineal incision and not allowed to rupture into the rectum or periprostatic tissues. Uncured prostatitis is frequently the underlying cause of recurrent urethritis, of infection transmitted to sex partners by men who had considered themselves cured, and is a possible focus of infection for arthritis, iritis and other inflammatory processes in distant parts of the body. Courses of prostatic massage and irrigation to anterior and posterior urethra should first be tried. These treatments should be given twice weekly for about one month followed by a rest of several weeks when further massage and irrigation may be found necessary if signs and symptoms justify. Gradual dilatation of the posterior urethra by means of metal sounds or the Kollmann dilator with or without instillations of silver nitrate solution in strengths of 1/10 of 1% may be undertaken in obstinate cases.

2. *Seminal Vesiculitis* is relatively common and should be treated on lines similar to those described above for prostatitis.

3. *Epididymitis.* Mild cases may be able to carry on when wearing a well fitting suspensory, most patients, however, experience such pain that it is necessary for them to stay in bed for a week or more when all intra-urethral treatment must be withheld. The scrotum should be well elevated and either ice or heat applied and sedatives prescribed to relieve the pain. Some patients are benefitted by the daily intravenous injection of 10 c.c. calcium gluconate for several days. A few of these cases pro-

gress to suppuration and will require surgical drainange. Treatment of vesicles and prostate should be undertaken only when all signs of acute inflammation in the epididymitis have disappeared.

4. *Periurethral abscess,* should be opened promptly when suppuration is established either through the urethral mucosa or externally.

5. *Cowperitis*—Suppuration of Cowper's glands may occur and require incision through the perineum.

6. *Arthritis*—Affected joints should be immobilized by light plaster splints, although passive movements done with extreme gentleness may help to prevent the formation of adhesions and subsequent ankylosis. The production of artificial fever by means of a hyperthermia machine in robust patients will frequently bring about rapid cures of this condition without any loss of joint function. The careful use of vaccines is sometimes helpful and the use of ultra short wave often gives rapid relief of pain. I have thought that the daily intramuscular injection of 10 cc. of a nonspecific protein Aolan, is of distinct value. The local focus which is usually prostate and vesicles should be given appropriate attention.

7. *Tenosynovitis and periostitis* should be treated along recognized lines. An exostosis on the os calcis begins as a periostitis is very painful and requires surgical removal.

8. *Conjunctivitis and iritis* are fortunately rare complications but if acute, should be regarded as serious, treated actively, preferably in hospital under the supervision of an ophthalmic specialist. The primary focus must not be overlooked.

9. *Endocarditis and septicaemia* are rare complications but very serious and frequently fatal. Treatment should be along recognized lines.

10. *Gonorrhoea of the Anus and Rectum.* This occurs quite rarely and yields readily to injections of 20% Argyrol twice daily.

The Technique of Irrigation.

As previously stated, potassium permanganate 1-800 at about 105° is the solution most commonly used. This should be delivered from a can containing one to two quarts at a height of about three feet. The nozzle must have a blunt conical tip and preferably have a shield to prevent splashing and a convenient cut off valve. The patient must void and then the nozzle is held against the meatus and the urethra allowed to fill with the solution. When comfortably full the solution is allowed to run out and then the urethra is filled again. This alternate filling and emptying of the canal is carried out until approximately half of the solution is used. Then if it is desired to irrigate the posterior urethra or bladder, the nozzle is held firmly against the meatus, the canal distended and the patient encouraged to relax the bladder spincter by breathing deeply, coughing or attempting to urinate, while the pressure is on. There is a certain knack in thus allowing the fluid to flow back into the bladder and care must be taken that no pain or soreness be produced by this procedure. Irrigations are rarely performed more frequently than once daily.

The Technique of Injection.

The solutions used are neutral acriflavin 1-200, argyrol or silvol 10%, protargol 0.5%, potassium permanganate grs. 2 to oz. 6. The syringe used must have a blunt conical glass or rubber tip. A convenient outfit is obtainable from any "Asepto" dealer, in which a suitable syringe is contained in a bottle which will hold enough for a day's use. Having voided, sufficient solution is injected to fill but not to distend the urethra and retained by pressure of the finger over the meatus, care being taken not to constrict the canal at any point and thus prevent satisfactory application of the solution to the whole urethra. Injections should be repeated from three to six times daily, depending on the severity of the discharge, the

solution should be retained in the urethra three minutes for permanganate and five minutes or longer for argyrol and other similar antiseptics.

Sulphanilamide Treatment of Gonorrhoea.

The use of sulphanilamide has been the most striking advance in the therapy of gonorrhoea in recent years. Its action is not specific to the diplococcal group of organisms, but the growth of many strains of colon bacilli and some of the staphylococci which are found as secondary infections in cases of prostatitis is also inhibited by this drug. While the earlier reports of cures in nearly 100 per cent. of cases in a few days are not justified by the facts, at the present time it would appear that at least sixty per. cent of cases are definitely benefitted by its use.

This drug is supplied by several reputable pharmaceutical houses in 5 and 7½ grain tablets. It is essential that only the product of a reliable manufacturer be used.

The following dosage is suggested for adults, expressed in grains per day. Fluids should be moderately restricted in order to maintain a sufficient concentration of the drug in the blood.

1st day—40 grains.
2nd day—60 grains.
3rd and 4th days—80 grains.
5th and 6th days—60 grains.

Thereafter 40 grains per day, which may be increased or diminished according to the patient's general reactions and the local signs. The daily dose should be divided into four equal portions most conveniently given after each meal and at bed-time. It is sometimes advantageous to give at the same time an equal amount of bicarbonate of soda. The drug should be continued in small doses for at least two weeks after the patient is apparently cured, otherwise one will have frequent recurrences. It is also suggested that local treatment be not abandoned in our enthusiasm for a new cure.

If laboratory facilities are available the dosage can be more accurately graded by administering the amount of sulphanilamide which will maintain a concentration of not less than 100 mgms. and not more than 150 mgms. per 100 cc. of urine, care being taken not to lose sight of any concurrent toxic effects upon the patient. The optimum concentration in the blood is 10 to 15 mgms. per cent. The technique for estimating the concentration in blood and urine will be found in many recent scientific articles. This drug is equally effective in children, administered in suitable dosage.

Signs and Symptoms of Sulphanilamide Intolerance.

Many patients complain of loss of appetite and a general feeling of listlessness as if a hypnotic had been taken, and more or less dizziness. While this is not of importance in the average case, it must be borne in mind that such a condition may constitute a serious occupational hazard if the patient works near unguarded machinery or on scaffolding or drives a motor car.

In some cases after a few days' treatment a bluish tinge may be observed in the skin and mucous membrane. Close observation will show this to be due to a discoloration of the blood, spectroscopic examination of which in most cases shows the presence of sulphaemoglobin, in other cases this discoloration is due to staining of the red blood cells by "aniline black." In most cases this complication although alarming to the patient and his friends, is not serious in robust individuals. If, however, a patient, whose normal haemaglobin is say, fifty per cent., has a further percentage of his red corpuscles rendered inactive by sulphanilamide or "aniline black" his oxygen carrying mechanism will be seriously impaired, demonstrated clinically by air hunger. With a view to lessening the chances of the occurrence of this complication, sulphur compounds should be eliminated as far as possible

from the diet and completely from the therapeutic treatment. For example, eggs and saline purges containing sulphates are forbidden. Constipation, however, must be avoided else sufficient hydrogen sulphide will accumulate in the bowel to promote the development of this complication. Some patients who have taken the drug for several weeks develop malaise and a high temperature without other signs. These symptoms disappear in a few days when the drug is withdrawn.

When the drug is given for long periods, regular leucocyte counts must be made, and treatment discontinued on the first indication of leucopenia, otherwise a severe agranulocytosis may occur which will, in all probability, be fatal. This destructive effect on the leucocytes is due to the benzine ring content of the drug and with this in mind it should not be given to men working in industries where they are exposed to benzine fumes or solvents; neither should it be given to luetic patients receiving arsenical treatment nor should patients using sulphanilamide be given barbiturates, although acetyl-salicylic acid is perfectly safe.

In a few cases of idiosyncracy a mild jaundice or even a severe liver damage has occurred. Glucose and sodium bicarbonate are the best antidotes.

As the drug is eliminated by the kidney, large doses must never be given to patients with renal insufficiency unless the patient can be in hospital, where the percentage of sulphanilamide in the blood can be estimated. This must be kept if possible between ten and fifteen mgms. per cent.

Standard of Cure.

In the case of acute gonorrhoea, such as we have been discussing in this paper, the determinator of a cure is usually fairly easy. However, it is imperative that sufficient consideration be given to this phase of the subject so that recurrences may be reduced to a minimum and that infected individuals, having easy consciences, may be prevented from spreading infection to uninfected sex partners.

No man, having had gonorrhoeal urethritis should be discharged as cured until all signs of inflammation have been absent for at least one month following cessation of treatment. That is to say there must be no urethral discharge, no pus in the prostate or adjoining glands. I feel that even in cases classed as "First Stage" as well as those in the second and third stages must have the prostate and vesicles examined before being discharged. It is generally accepted that fewer than ten pus cells in a high power field of the microscope, is normal prostate fluid. However, it is advisable that any suspicious urethral moisture, any shreds in the urine, as well as suspicious prostatic secretion be subjected to repeated smears and culture. Having made this outlined examination, it may be considered safe to discharge the patient as cured.

A final word, having nothing to do with the treatment of gonorrhoea, but nevertheless of paramount importance in properly dealing with all gonorrhoea cases: Be *"Syphilis Conscious."* Every case of gonorrhoea is a candidate for syphilis, a much more serious, more deadly, more insidious disease. *Look out for syphilis;* examine every sore on the genitals by the dark field method at the earliest possible moment and do repeated blood tests for syphilis on all cases of gonorrhoea, even where no suspicious signs of syphilis are seen.

It is your duty as physicians to deal with sick people in two ways. First from the point of view of the proper diagnosis and treatment of the particular disease, as it affects its victim, and second, from the point of view of the relation of that infected person to other individuals in the community. Gonorrhoea is our most prevalent serious, contagious disease. There are said to be well over one million new cases of gonorrhoea in the United States every

year and the disease is probably almost as prevalent here in Canada. So be prepared; your first private patient may be a man smitten by the gonococcus. Give that patient your serious thought, diagnose his case carefully, explain the necessity of correct care and treatment, treat him thoroughly, and finally use every available means to establish a cure.

APPENDICITIS

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In discussing the subject of appendicitis most text books describe a series of symptoms and signs, in the presence of which one could hardly fail to make a diagnosis. Yet one often hears a final year student at the end of his trimester on surgery remark that he has yet to see a "typical" case of appendicitis, and in the next breath ask how can one diagnose that treacherous disease with certainty? Actually, since appendicitis is by far the commonest acute abdominal emergency met by practitioner and surgeon alike, the practice of medicine and surgery would lose much of its interest if the diagnosis were an easy, routine prelude to appendicectomy.

It is because this question comes up so frequently, and because a group of patients come to hospital, who, in spite of a doctor's care and best efforts, have progressed to a stage where the diagnosis is no longer "appendicitis" but "peritonitis" that one is tempted to add one more to the lengthy list of publications on this difficult subject —admitting freely, however, that there is no royal road to the diagnosis in many cases. By a brief discussion of the etiology and pathology it may be possible to somewhat clarify the symptomatology and diagnosis.

Etiology

Much has been written concerning the etiology of appendicitis, implicating anatomical, bacteriological, racial, dietary, and many other factors; but in considering appendicitis as it is seen in this country two factors stand out—obstruction and infection. Since the latter is always potentially present, the appendicial contents being contaminated with organisms, the former is the primary etiological factor, and when present, provides the circumstances under which the organisms may invade the mucous membrane—which in health functions as an efficient barrier to their passage.

What is the evidence that obstruction is an important etiological factor? It may be summed up as follows:

The text books of anatomy state that in the majority of subjects the appendix is a free-lying organ, and this is confirmed if one examines the appendix at autopsy or at operation in individuals who have never had symptoms of appendicitis. In contrast to this, one finds in operating on a group of patients with acute appendicitis that in a large proportion the appendix is retrocaecal, or kinked, or bound down by a peritoneal fold in such manner as to facilitate obstruction; or there may be an actual obstructing agent in the lumen in the form of a faecolith or even a foreign body. That obstruction is actually present at the time of operation is confirmed by the tension in the distended organ.

Interpretation of a very common type of history also reveals evidence of an obstructive phase in the development of a case of appendicitis Frequently the earliest symptom is that of

crampy distress referred to the umbilicus or just above it, and this is the subjective evidence of obstruction.

One may think too of the analogy of Meckel's diverticulum, which has much in common with the appendix, including in a certain proportion of cases a tendency to become acutely inflamed and to perforate. The cases which show this complication are those in which the base is narrow, and for this reason, or due to a kink or a twist, become obstructed; so much so that when a Meckel's diverticulum is found by chance, most surgeons do not remove it if it has a wide base and is lying free.

Finally there is experimental evidence. Wells, working with young rabbits, in which the appendix resembles that found in the human, discovered that acute appendicitis could not be produced, unless the appendix was obstructed.

It may be objected that appendicitis may occur on the absence of any kink or twist in the appendix, and that in those cases which show such a peculiarity the situation has existed since birth, while the attack of inflammation may not supervene until late in life. The answer is that the appendix, being a narrow tube with a relatively thick and indistensible wall is by its structure prone to become obstructed. A fixed kink in the course of the organ merely makes obstruction more likely. The narrowness of the tube is a predisposing factor toward obstruction, the exciting factor is anything which causes oedema of the mucous membrane, such as a period of constipation with the accompanying irritation to the mucosa, or a mild and perhaps unrecognized enteritis due to a dietary indiscretion or an upper respiratory infection.

Once obstruction has occurred there is a train of events identical with that which follows obstruction elsewhere in the intestinal tract—spasm, increased peristalsis, congestion of veins and lymphatics, oedema, invasion of the oedematous wall by organisms, ulceration of the mucosa, thrombophlebitis of the smaller veins going on to involve the appendicular vein and artery, gangrene and perforation — the whole process being, however, accelerated by the relative indistensibility of the small closed cavity in which it is taking place.

Pathology

The pathology of the developing inflammation in the appendix has been briefly outlined in the foregoing discussion of etiology, but it may be of value to discuss in somewhat greater detail the complications which may arise as the pathological changes progress further, remembering that it is the complications of the process in the appendix which constitute a danger to the patient.

While the acute inflammation is affecting the appendix and organisms are invading its wall, the other structures in the immediate neighbourhood also are reacting. The peritoneal covering of the surrounding small intestine and caecum becomes congested and oedematous, and an exudate containing fibrin is thrown out, which, if in sufficient quantity serves to glue the nearby loops of bowel together. The greater omentum in its wanderings about the abdomen may be implicated and also become oedematous and adherent. If the particular type of infection which is present proceeds slowly enough, and elicits sufficient fibrin response, by the time perforation occurs, the appendix will be clothed with a mass of oedematous and adherent bowel and omentum, and even though the integrity of the appendix is destroyed the process remains local. An appendiceal *mass* has been formed.

In certain cases, again depending on the response of the individual to the particular organism involved, the natural defenses of the body will at this stage overcome the infection, and resolution will occur without any actual abscess being formed.

In others the infection will progress,

and in the centre of the mass suppuration will occur, the result being an appendiceal *abscess*. Like any other abscess it has a tendency to point, and the most constantly present hollow viscus, and the most vulnerable, because it is acutely inflamed, and in every way the most likely place for spontaneous drainage, is into the caecum. Here the pus will become unrecognizably mixed with feces, and the attending surgeon may never realize why the conservative treatment of an appendiceal mass has been followed by such spectacularly fortunate results.

Failing spontaneous drainage into the caecum the abscess may point into the rectum, colon, vagina, small bowel or bladder, or very rarely through the skin; and none of these possisble events would be a tragedy. However, a patient in whom an appendiceal mass has become an abscess is continuously faced by the possibility of one almost certainly fatal complication, namely that the abscess may point and rupture into free peritoneal cavity, suddenly flooding that cavity with highly infected pus. The almost inevitable outcome is early death from fulminating peritonitis. It is to protect the patient from this last unhappy complication that one must recognize the presence of abscess as opposed to mass and decompress the abscess by drainage.

To go back to the developing inflammatory process in the appendix. Due to the particular type of infecting organism and the patient's lack of response to it, events in the appendix may move with such speed that perforation occurs before the protecting fibrinous adhesions have formed, and at once a peritonitis is set up, beginning in the immediate neighbourhood of the appendix, and spreading thence to involve the pelvis and eventually the whole abdominal cavity, with resulting toxaemia and ileus.

Even this may be survived, with or without drainage of the abdomen, but of those individuals who survive, a certain number will develop a residual loculation of pus, in the pelvis, under the diaphragm or elsewhere in the abdomen, which if undrained may rupture spontaneously. Early recognition of such an abscess and drainage will materially improve the patient's chances of recovery.

Symptoms and Signs

The early stage of the disease, when conditions in the appendix are characterized more by obstruction than by inflammation is accompanied by crampy distress related to the umbilicus or epigastrum, in keeping with the general rule that visceral pain is related to the mid-line. Reflex anorexia and vomiting may occur at this stage.

When inflammation becomes established and the peritoneum clothing the appendix and adjacent organs becomes involved, the pain shifts to the area in which the appendix lies, and becomes steady. The shift in the location of the pain indicates inflammation of the peritoneum of the abdominal wall.

Tenderness is the primary physical sign, and is related to the part of the abdomen in which the appendix lies — usually the right lower quadrant. Even in the earliest phase of obstruction, without significant infection, deep palpation will elicit tenderness, probably because the pressure of the examining hand increases the tension in the distended organ. As the peritoneum becomes involved it becomes sensitive and tenderness more acute.

Hyperaesthesia is frequently present and in some manner appears to be related to the tension in the distended appendix, because it is more constantly present before perforation than after.

True rigidity is relatively infrequently present and is in proportion to the degree of involvement of the peritoneum of the anterior abdominal wall, tending to be absent when the appendix is retrocaecal and present in acute

cases in which the appendix lies within the peritoneal cavity.

Rebound, or referred tenderness is a valuable sign, and is quite constantly present in acute cases. Its demonstration depends on conveying a mechanical impulse to the contents of the right lower quadrant, with resulting pain referred to that area. This is frequently done by making steady pressure on the left side of the abdomen and then suddenly releasing the examining hand. A preferable method, more delicate and more specific, is that of using the diaphragm to jar the contents of the abdomen by asking the patient to cough, or in well-marked cases, merely to sniff. When this test is positive, it with certainty indicates peritoneal inflammation in the area to which the pain is referred, whereas other conditions such as retroperitoneal inflammation will give a negative test.

It is of interest to enquire into the pathological physiology of this test. In health one may stimulate the abdominal contents violently by cough, or even by blows upon the abdomen, without pain; and yet when inflamed, the peritoneum becomes exquisitely sensitive to the slightest mechanical stimulus. The situation is analogous to that obtaining in a joint, such as the knee. Under normal conditions one may run and jump and otherwise traumatize the joint without pain, but in the presence of acute inflammation the nerves of the synovial membrane become sensitive in the extreme so that the slightest movement results in severe pain.

Rectal tenderness has the same significance as abdominal tenderness, but examination by this method has the advantage that the examining finger is introduced inside the abdominal wall, so that local conditions in the abdominal wall, such as inflammation, rigidity or hyperaesthesia are obviated. Also it affords a more direct examination of an appendix lying low in the pelvis.

Up to the point of perforation the actual amount of tissue involved in the inflammatory process is small and the infection is localized, so there is very little reaction in temperature. A careful temperature, taken per rectum, may show an elevation of a degree or less, or it may be normal. The pulse too shows little, if any, elevation.

The white blood count is usually elevated, but like all the other symptoms and signs, it is subject to wide variation. Not uncommonly one sees an acutely inflamed, or even gangrenous appendix removed from a patient who has shown a normal white blood count. The count is particularly likely to be low in those cases of appendicitis which follow a general infection of the influenza type, which is frequently associated with leukopenia. Perforation of the appendix with general peritonitis may be accompanied by a rapid fall in the white blood count as the leucocytes are thrown out into the peritoneal cavity more rapidly than the supply can be replenished.

Diagnosis.

The first principle to remember in attempting to diagnose appendicitis is that there is no one symptom or sign which is constantly or reliably present. Some patients are not sensitive to visceral stimuli and are unaware of any crampy pain, others do not vomit or even lose appetite, just as some people can cross the Atlantic Ocean without anorexia or vomiting. Even tenderness may be unreliable due to the position of the appendix, or because it is gangrenous and insensitive, or because of the patient's high threshold for pain.

There are, however, certain rules that are helpful. Appendicitis is the commonest cause of abdominal pain associated with signs of peritoneal irritation. A history of previous attacks of pain, particularly if those attacks have been accompanied by vomiting, suggests appendicitis. Pain which begins in the upper abdomen and shifts to the lower abdomen is likely to be due to appendicitis, while in such con-

ditions as salpingitis the pain commences in the lower abdomen and may possibly spread later to the upper abdomen. A normal or slightly elevated temperature, associated with a significant rise in white blood count, in the absence of signs of intraperitoneal haemorrhage is likely to mean appendicitis.

It is useful to consider that the information available may be divided into three parts—history, physical examination, and laboratory findings (including temperature), and that if any two of these are in keeping with appendicitis the patient should be considered to have that disease unless there is another explanation for the findings.

Nowhere in surgery is one as apt to encounter red herrings as in investigating a case of appendicitis, and if one is misled the results may be tragic. The presence of pus or blood in the urine may be due to pre-existing urinary infection, or because an acutely inflamed appendix is lying in close proximity to the right ureter or bladder. Appendicitis may occur in association with any other disease or condition; for example, pneumonia, pregnancy, acute nephritis or diabetes, and in patients who are confined to bed the onset may be insidious with a striking absence of pain. The first complaint of pain may signify perforation.

Finally, there is notorious difficulty in distinguishing certain cases of appendicitis from salpingitis. In this regard it is well to remember that menstruation does not confer immunity to appendicitis, so that pain during this period does not necessarily indicate salpingitis. Again, just as salpingitis may cause irregularities of menstruation due to involvement of the ovary in the inflammatory process, so also may a low-lying appendix cause perioophoritis with resulting disturbance of the cycle. If it is remembered that the appendix and the Fallopian tube are two rather similar tubular structures, occupying the same general area of the abdomen, and possibly even in contact with one another, and that just as salpingitis may be associated with periappendicitis, so may appendicitis be associated with perisalpingitis and oophoritis; then one must admit that in some cases the distinction cannot be made with certainty. In case of doubt it is less dangerous for the patient to have an acute salpingitis looked at, than an acute appendicitis neglected. .

Treatment.

Difficulty and controversy arise only in the treatment of the complications of appendicitis. It is agreed that when a diagnosis of appendicitis is made and there is no evidence of perforation, the correct treatment is to protect the patient against the dangers of peritonitis by removal of the appendix at the earliest opportunity. The McBurney incision gives the most direct approach with least danger of soiling clean peritoneal cavity and interferes least with the integrity of the abdominal wall, so is the incision of choice.

The complicated cases may be divided into two groups—those with evidence of a mass, and those with general peritonitis. Both these groups have this in common, that they have been ill for days rather than hours, have endured pain, and probably have been vomiting, so are likely to be dehydrated and in need of a rest. There is no longer anything to be gained by speed, and whatever other treatment is to be carried out time should be taken to improve the patient's general condition. Water and salt are supplied in appropriate amounts by intravenous, with glucose if there is evidence of acidosis, and rest is provided, if necessary by sedatives.

First let us consider the treatment of those patients who show evidence of a mass when first seen. By forming a mass these patients have demonstrated that they react favourably to

the infecting organism, and if on the one hand, the surgeon does not break down the protecting barrier of adhesions by ill-advised efforts to remove the appendix, nor on the other fail to recognize the development of an abscess and allow it to rupture into the peritoneal cavity—the outlook is good. To begin with, the patient is given an opportunity to handle the situation himself. He is put to bed in Fowler's position, heat is applied to the abdomen by electric cradle, the intestine is kept at rest by giving no food by mouth, and above all, no laxative, while fluid balance is maintained by intravenous administration of saline or glucose. Sedative is given only in minimal amounts. If, as happens in more than half the cases, the patient improves steadily under this regime, as evidenced by subsidence of pain, falling temperature and pulse, and decrease in size and tenderness of the mass, the treatment is continued until the mass disappears. The patient is then discharged with strict instructions to return at the end of three months for appendicectomy, or immediately, if there is recurrence of symptoms before the three months period is up. The remarkable thing is that when appendicectomy is performed the appendix frequently shows only a little fibrosis

A proportion of the patients with a mass will not react favourably, but will show continued pain, fever, and tenderness with enlargement of the mass, and this is evidence that the process is not resolving, but has gone on to form an abscess. In view of the dangers mentioned above, it becomes the duty of the surgeon to recognize the situation early and protect the patient by decompressing the abscess by drainage. Occasionally this may be done through rectum or vagina, more often an abdominal incision is necessary, an attempt being made to enter the abscess directly, without opening free peritoneal cavity. Drainage is maintained by rubber tubes or, if preferred, by gauze. It is important that the surgeon remember that he is operating to drain an abscess rather than to remove an appendix. Any effort to remove the appendix may break down the fragile barriers that nature has erected and again expose the patient to the dangers of peritonitis. These patients also should return in three months for appendicectomy.

Finally we must consider what can be done to assist that group of patients who, when first seen, are desperately ill with generalized peritonitis. The situation is usually not hard to recognize—a history of abdominal pain of thirty-six hours or more, a drawn, anxious face, circum oral pallor in young patients, a dry tongue, diffuse abdominal tenderness with more or less rigidity, possibly signs of free fluid, marked rectal tenderness, a rapid thready pulse, fever of 102° or 103° and a white blood count which may be high or low, depending on how rapidly the cells which are being lost into the abdominal cavity can be replaced.

At the outset one must realize that the stage when the surgeon can intervene and greatly modify the course of events is past. It is now largely up to the patient and his ability to withstand and overcome the infecting organism. The most valuable assistance that can be given him in this fight is by general supporting measures—rest, fluids, heat, Fowler's position, a duodenal tube to keep the stomach and small intestine empty, and in some cases chemotherapy in the form of one of the sulphanilamides.

The question remains—will the patient's chances be improved if the appendix is removed and the abdomen drained? From clinical experience, and on theoretical grounds most surgeons agree that the appendix should be removed, after the patient's condition has been improved by a few hours general treatment. The peritoneum is a living membrane with wonderful defensive powers, and is fighting desperately, by throwing out exudate and

forming fibrinous adhesions. The one structure which not only is not actively fighting but is acting as a culture medium for fresh crops of organisms is the gangrenous and perforated appendix. In addition there may be actual continuity with the caecum allowing continuous faecal contamination of the peritoneum. With this pathological picture in mind it seems reasonable to believe that the patient's chances will be improved by removal of the appendix, provided that it is done expeditiously and gently so as not to further abuse the peritoneum by adding trauma to infection. The cavity is then drained, and supportive treatment continued. The surgeon must remain on the alert to recognize and treat that very common further complication, a residual abscess, which may develop in the pelvis, or under the diaphragm or elsewhere in the abdomen.

In conclusion one may remind the reader that patients do not die from appendicitis, but from the complications of appendicitis, and that almost all the fatalities are in the group with perforation and general peritonitis. Once a patient enters that group he faces a 20% to 25% chance of dying in spite of any known form of treatment. The obvious answer is that it is our duty to educate the public to take abdominal pain seriously, and for our own part to be ever alert to recognize appendicitis in its early stages. Since there is no reliable method of assessing the degree of inflammation present, and in this regard the signs may be grossly misleading, it is our further duty to remove the organ as soon as possible after a diagnosis of appendicitis is made, unless appendicectomy is contraindicated for one of the reasons discussed above.

HEPARIN

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The advantages of an anticoagulant which is active in vivo and can be used without toxic effects have long been appreciated. Hirudin or leeches have been used but various disadvantages connected with their use prevented any extensive application. The early workers on the chemistry of blood clotting in the last century, notably Schmidt, reported that after previous alcoholic extraction of tissues, aqueous extraction yielded a potent anticoagulant. W. H. Howell of Johns Hopkins was the first to undertake an extensive study of this anticoagulant. He succeeded in preparing the substance which he named "heparin" from dog liver. Howell showed that the purified material had a remarkably high potency, was relatively non-toxic on injection, and that the anticoagulant was probably a normal physiological substance. While his work definitely indicated the importance of this substance and led to a number of investigations, the costly process of preparation prevented any wide application. By extensive modifications of Howell's method, Dr. Charles and Dr. Scott of the Connaught Laboratories, who undertook this work at the suggestion of Professor Best, in 1933 developed a commercial method for the purification of heparin and thus made possible studies of its application. In 1936 they succeeded in isolating the active substance as a crystalline barium salt. Pure heparin is thus now available and is being used in the various researches on heparin in this University. Its potency is 100 units per mg. The unit as originally defined by Howell was the

amount of heparin which would keep 1 cc. of cat's blood fluid in the cold for 24 hours. It has been suggested that a more permanent standard would be the potency contained in 1/100 mg. of the material from which the barium has been removed.

Chemistry.

As Howell originally found, heparin is carbohydrate in nature. It resembles a mucoitin sulphuric acid as the presence of glucosamine, glycuronic acid, acetic acid and sulphuric acid has been demonstrated. The anticoagulant action is associated with the sulphuric acid groups. Sulphonation of other polysaccharides, such as cellulose, yields anticoagulants. Various synthetic anticoagulants in use such as Liquoid Roche, Chicago blue, etc., are also sulphonic acids although none of these are as active as heparin. The high potency of heparin is not due to the sulphuric acid group alone as removal or blocking of the amino group decreases its activity. The large number of sulphuric acid groups means, as Jorpes has pointed out, that heparin is the strongest naturally occurring organic acid known. As would be expected, heparin forms salts with the basic groups or proteins. The salts formed with the basic proteins, particularly the protamines, are of special interest as they have an extremely low solubility. Hence the protamines can be used to precipitate heparin both in vitro and in vivo and this reaction provides a simple means of testing for heparin. Since protamine itself has a slight anticoagulant action, a decreased clotting time on addition of protamine to blood indicates the presence of heparin: the amount of heparin present can be determined by finding the amount of protamine giving the shortest clotting time. Three milligrams of protamine is equivelent to 1 mg. (100 units) of heparin. Chargaff and Olson, who originally described the reaction, have suggested using it in vivo to remove heparin from the circulation.

The assay of heparin.

The potency of heparin preparations is determined by biological assay. As with all biological assays, the potencies of the unknown and a standard preparation are compared under the same conditions. Two methods of comparison are available for heparin assays. The first is the determination of the least amount of heparin which will keep blood stable under certain conditions, the second consists in determining the effect of the heparin on the clotting time of blood. The first procedure was applied by Howell in the original method of the assay of heparin and consisted in determining the least amount of the heparin solution which would keep 1 cc. of freshly drawn cat's blood fluid in the cold for 24 hours. The potency of the unknown is calculated from the ratio of the dilutions of unknown and standard required. Fischer has used the second type of assay, determining the clotting times obtained with varying dilutions of standard and unknown.

Because of the inconvenience of using fresh blood and the wide variation in the value of the end-point in different animals with resulting difficulties in the assay, attempts have been made to substitute other artificial clotting systems. Decalcified blood or plasma has been used for the test and clotted with calcium and kinase or thrombin. Both plasma and kinase are very unstable when tested in the assay. Hen plasma appears to be more stable than mammalian plasma in this regard and has been extensively used by Fischer and others. In any method of assay it is necessary to keep the temperature and salt concentration the same for standard and unknown, as the activity is markedly affected by them.

Distribution.

Heparin can be extracted from all the vascular tissues. Liver, lung, and intestine contain the largest amounts:

about 1,000 units (10 mg.) per 100 g. Muscle, heart, kidney and spleen contain less—about 200 units (2 mg.) per 100 g. Brain contains less and blood only traces. There appear to be species differences both in the absolute amount present in a tissue and also in the relative distribution among the tissues. The values given are for the dog.

Interest has been recently taken in the histological distribution of heparin. Jorpes and co-workers have found that the metachromatic violet colour with toluidine blue given by mucoitin and chondroitin sulphuric acids is highly specific for heparin. This suggests that the Ehrlich's mast cells which contain granules with this staining property are the chief source of heparin. The mast cells are chiefly localized in the vascular system, being found in the vessel walls and surrounding connective tissue of the liver and other organs.

Only traces of heparin are found in blood normally. Valuable evidence as regards the physiological rôle of heparin would be the finding of fluctuations in the heparin content of blood in various pathological conditions. Up to the present this has been established for only one condition, that of anaphylactic and peptone shock in the dog. In anaphylactic shock in the dog, one of the outstanding symptoms is the incoagulability of the blood. Using quite different methods for studying the problem, Howell, Quick, and Waters, Markowitz and Jaques have all concluded that the long clotting time is due to the presence of large amounts of heparin in the circulation. The last group used protamine to titrate the amount of heparin. In liverless animals, in which all the symptoms of anaphylactic shock were produced, almost no increase in the heparin in the circulation was found. Assays of the heparin content of the livers of the shocked dogs also showed that the heparin in the blood came from the liver. As much as 1/3 of the heparin content of the liver was present in the blood.

Action on the Clotting System.

There has been considerable controversy in regard to the nature of the anticoagulant action of heparin. Howell found that heparin acted as an antithrombin, but only in the presence of an unknown labile factor present in plasma. This has been confirmed in other laboratories. The factor responsible is non-dialyzable, destroyed by heating to 60° C., and is probably protein. It is found in the albumin fraction of plasma, but it is not serum albumin.

Quick has shown that other anticoagulants, such as the synthetic dyes, also act as antithrombins in a manner similar to heparin. Quick suggests that heparin does not act directly as an antithrombin but that it combines with the normal antithrombin of plasma and serum, thereby greatly increasing the affinity of the antithrombin for thrombin. The normal antithrombin of plasma and serum has long been known, being first reported by Morawitz in 1904 and it also appears to be associated with the albumin fraction. It is responsible for the rapid disappearance of thrombin from serum. Its low affinity for thrombin, compared with that of fibrinogen, results in its having little anticoagulant activity.

As Howell pointed out, heparin might also conceivably act as an antiprothrombin but that this hypothesis cannot be tested until some test for thrombin other than the clotting of fibrinogen can be devised. The effect of heparin on platelets which is probably an important part in its anticoagulant action is referred to later in this paper.

The Effect of Injections.

On intravenous injection heparin produces a long clotting time. With pure heparin this is the only known effect, the substance being completely non-toxic. Subcutaneous or intraperitoneal injections, unless very large, have no effect on the clotting time of larger animals, but they are quite ef-

fective in small animals like the rat and the rabbit and are the most satisfactory methods of administration for these animals. The relationship between clotting time and heparin concentration in the blood in vitro is not linear but is of the form $t^c = B[1 + (Ax)^p]$ where t= clotting time, x= heparin concentration, c, B, A and p are constants. Hence it takes a definite concentration of heparin to raise the clotting time above normal, whereas small increases above this cause a marked increase in the clotting time.

The clotting time after intravenous injection returns rapidly to normal so that a dose of 350 units per kg. in the dog (sufficient to render the blood incoagulable) completely disappears in 1½ hours. The injected heparin is probably destroyed by the liver as it is not excreted nor stored in any tissue. The rapidity with which injected heparin is destroyed makes the administration of heparin by single intravenous injections an expensive and dangerous procedure as the clotting time oscillates rapidly from over 24 hours to normal. As is to be expected, however, the rate of destruction increases with the concentration of heparin in the blood. Hence it is possible to maintain a constant concentration of heparin in the blood (i.e., a constant clotting time) by means of a continuous injection, a constant level being obtained when the rate of destruction equals the rate of injection. By giving a single injection at the same time as the continuous is started, the level can be reached more quickly. This is the most satisfactory method of administering heparin if the animal is to be kept under the influence of the anticoagulant for any period of time. With a technique devised by Jacobs of Chicago, it is possible to keep dogs heparinized for days without discomfort (heparin is injected into the jugular vein through a tube in a covered cable attached to a universal joint at the top of the cage): 35 units/kg./hr., with an initial injection of 35 units/kg., is a satisfactory dose. The rate of destruction for a given concentration is remarkably constant from dog to dog, so that the amount of heparin in the blood for a given rate of injection is constant, but the resulting clotting time varies considerably due to variations in the clotting system in different animals. When the concentration of heparin in the blood reaches a value of 2 units per cc. the rate of destruction becomes constant and hence the technique described above has to be modified. However, up to the present we have not found it necessary to use concentrations of this order as much smaller amounts provide adequate protection for even drastic operative procedures. All the values mentioned here are for the dog and, of course, will only be roughly approximate for other species.

The Physiological Significance of Heparin.

The data cited above suggest that heparin is a normal physiological substance. Since blood contains only traces of heparin (0.1 units/cc. in the dog) the latter is probably not the chief factor in the maintenance of the fluidity of the blood, although its concentration in the blood, like that of kinase and prothrombin, affects the clotting time of the animal. The fact that it is released in large amounts from the liver in shock might suggest that the secretion of heparin into the blood may be one of the normal functions of the liver. Mellanby suggests that the physiological rôle of heparin is to keep the blood fluid by preventing local clotting in the vessels due to the leakage of kinase into them from disintegrating tissues. The location of heparin in the mast cells, which are found mainly in the walls and surrounding connective tissue of the blood vessels of the liver and other organs, strongly suggests this.

Laboratory Applications.

The many possible applications of heparin in the laboratory are obvious.

They can be divided into two classes, uses in vitro and uses in vivo. Heparin is used in vitro to preserve the fluidity of the blood because of its extremely high potency which frees it of the objectionable features of the decalcifying anticoagulants. Further, since it is non-toxic, it can be mixed with the blood by injecting it into the animal, which is a valuable point of technique for some purposes. Its chief use in vivo is to prevent intravascular clotting since it is equally active in vivo and in vitro. The various applications of heparin up to the present will be summarized under these headings.

Oxalate and citrate have the disadvantage as anticoagulants that they must be used in relatively high concentrations. Hence, either the blood must be diluted with the anticoagulant solution, or a concentrated solution or the solid anticoagulant added. In the latter case the plasma becomes hypertonic with removal of water, lipids and other substances from the cell. The net result in both cases is to introduce an error into the plasma-cell ratio and into all analyses of either plasma or cells or analyses comparing the two. A further disadvantage of the decalcifying agents is that they affect the red cell membrane. Olmsted originally observed this in regard to the permeability of the membrane to sugar. This is also seen in the fact that citrate and oxalate affect the sedimentation rate of the red cells in haemophilic blood. As heparin does not, it has been suggested that the rate obtained with heparin is the true one. Because of these advantages heparin has been recommended for a number of routine analyses, such as plasma lipids, phospholipids and cholesterol. It has the advantage that it can be used for such analyses as blood calcium where the decalcifying agents cannot be used. Heparin is also of value in diluting fluids for cell counts, particularly for platelet counts.

Another application of heparin in vitro is in blood transfusion. The heparin, of course, can be given to the donor and the transfusion performed either directly or indirectly. The heparin received by the subject is rapidly destroyed. This has been applied clinically by Clemens and others. The most striking experimental application of this is in the experiments of Thalhimer, Solandt and Best on experimental uraemia. A double pump connecting the circulation of two dogs provided an exchange of blood between them at a rate of 12 litres per hour. Clotting in the apparatus was prevented by the use of heparin. In the actual experiments one dog had been nephrectomized a few days previously and had a high blood urea (200 mg. per cent.) and was in coma. When connected to the donor, the blood urea fell rapidly approaching the normal value, the kidneys of one dog serving satisfactorily for both for the duration of the experiment.

The use of heparin in vivo to prevent intravascular clotting brought about by various agents, such as micro-organisms, has not as yet received wide application but it does suggest many interesting possibilities. An interesting application of this is its use by Widström to prevent the formation of adhesions in experimental pleurisy.

The chief use of heparin in vivo, however, is in the prevention of various forms of thrombosis. Since the formation of a thrombus is essentially an agglutination of platelets, there appears to be no *a priori* reason for assuming that heparin, which affects the clotting system, should have any effect on thrombus formation. Howell, however, suggested that heparin might increase the stability of platelets and hence affect thrombus formation. The work of Murray, Jaques, Perrett and Best, and of Best, Cowan and MacLean, has definitely shown that heparin does affect thrombus formation and appears to be as potent in this regard as it is as an antithrombin. The Toronto workers have shown that the formation of typical thrombi produced experiment-

ally and consisting almost wholly of platelets could be completely prevented by the administration of heparin. The first group produced the thrombi in peripheral veins by crushing the intima on a thread passed up the lumen with haemostats, or by injecting sodium ricinoleate into the vein. The second group produced the thrombi by a technique originally described by Rowntree and Shionoya. The artery and vein of a limb were joined by glass cannulae with a small glass cell placed between. As the blood entered the cell, large numbers of white thrombi formed, sufficient in time to plug the cell. Heparinizing the animal kept the cell completely free of thrombi in the case of dogs, cats and monkeys. Rabbits caused some difficulty, as their platelets are more fragile, but with a sufficiently large dose the cell could be kept free of thrombi. Recently Fidlar and Waters have observed that the use of heparin in the heart-lung preparation results in the complete preservation of the platelets in spite of the very large foreign surface area (rubber tubing, etc.) to which the blood is continually exposed. Two hours after the operation the blood showed a normal platelet count and perfectly normal platelets. It is possible that this power to stabilize platelets may be an important part of the anticoagulant action of heparin. Since heparin prevents thrombus formation it may prove of value in coronary thrombosis. This has been investigated in animals by Solandt and Best. The thrombosis was produced by injecting sodium ricinoleate into the left coronary artery of the dog and the progress of the thrombosis was followed by means of the electrocardiogram. Administration of heparin completely protected the animal from thrombosis.

Another application of heparin in vivo is as an adjunct in blood vessel surgery. It has been found (Murray and Best) that satisfactory results may be obtained with a simplified technique if heparin is used after the operation to prevent thrombosis. This technique should widen the experimental application of blood vessel surgery.

This paper has been purposely limited to the experimental aspects of the heparin problem. Clinical applications are at present largely in the experimental stage, but are in general an extension of the laboratory results described.

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ENDOMETRIOSIS

By BARBARA WATTS, '39.

This disease is a condition of misplaced mullerian mucosa of uterine or tubal type, in or upon pelvic structures. Various terms, such as adenomyoma, mullerianoma, endosalpingiosis, have been used by different writers, but the one most common to-day is endometriosis. The disease is becoming more widely recognized so that in the last few years it has ceased to be a curiosity and numerous series of cases have been reported in the literature. The essential cause of the condition, however, still remains unproven.

Theories of Origin

1. *Development of Displaced Mullerian or Wolffian duct Tissue.*—Von Recklinghausen in 1896 published one of the first reports on the disease. His theory is based on the fact that embryologically the Mullerian and Wolffian ducts cross. He believed that at this point remnants of one or the other may remain and later develop into glandular tissue.

2. *Invasion Theory.*—In 1896 Cullen began to observe the condition in the uterus and in 1908 published a monograph on the subject with an analysis of nearly a hundred cases. His observations led him to believe that adenomyoma of the uterus was due to normal mucosa flowing into chinks in a diffuse myomatous thickening of uterine muscle. He stated that the cause of the invasion was unknown.

3. *Theory of Serosal Heteroplasia.*—In its original form this was advanced by Ivanhoff in 1898. In its present form it postulates that endometrial implants are the result of metaplasia of the serosa of the peritoneum. possibly an end result of inflammation or ovarian stimulation. It is capable of wide application and has mnny advocates, among them Mever. Novak and Lauber. A review of embryology shows that both the ovary and mullerian ducts are derived from a modification of coelomic epithelium. Consequently endometrium, endosalpinx and ovarian epithelium are simply degrees of differentiation of coelomic epithelium. Should some undifferentiated cell rests remain anywhere in the pelvis these might be stimulated by inflammation (Meyer) or ovarian secretion (Novak) to develop into endometrial tissue.

4. *Implantation Theory.*—Although cases of ovarian endometriosis had been observed since 1899 by Russell, Semmelink and Cullen, the significance of these lesions was not appreciated until Sampson's classical paper on "Perforating Haemorrhagic Cysts of the Ovary" in 1921, in which he advanced the theory that this perforation may give rise to implantation adenomas of the peritoneum. He brought forward histological evidence that the cyst lining was similar to adenomyoma of the uterus. At this time he believed that the only cause of peritoneal endometriosis was the implantation of epithelium conveyed from the lining of these ovarian cysts in the menstrual blood spilt at perforation. But subsequently he observed that peritoneal endometriosis frequently occurs without demonstrable mullerian mucosa in the ovary, and in 1922 he extended his views, stating that tubal and uterine epithelium at times escapes through the tube into the peritoneal cavity in the menstrual blood. This lodges where most expected, on the nearest available place, particularly on the lateral surface of the ovary, on its free border and in the pouch of Douglas. It may lodge only on the ovary, only in the pelvis or in both. His evidence for this theory of ovarian endometriosis is the following — (1) the lesion is found on the part of the ovary most exposed to exudate from the tube. (2) the tube is patent in practically all cases studied.

(3) epithelium of cysts is often ciliated. He considers the ovary is an intermediary host which may impart greater virulence to epithelial cells developing on it but may not be essential for the development of peritoneal endometriosis. A little later Jacobson demonstrated in rabbits and monkeys that similar peritoneal lesions could be produced by scattering bits of uterine mucosa in their peritoneal cavity. Novak's objections to the theory of dissemination through the tube is based on a study of several hundred Fallopian tubes. Seven of these contained bits of uterine mucosa but these appeared too large to have entered the tube by the very narrow intramural portion. The objection is also raised that the tube is a funnel shaped structure, with the widest mouth at the ovary and peristalic waves and cilia directing substances in the lumen towards the uterus. It is questioned that particles of dying, cast-off endometrium can live long enough to travel up the tube and implant themselves on the ovary.

5. *Other Theories.*—Sampson has also suggested that the dissemination of pelvis endometriosis may be through venous or lymphatic channels, since he has observed bits of endometrial tissue in these situations. This theory is also advanced by Halban.

Schiller suggests endometriosis is a result of metaplasia of lymphatic epithelium.

Direct transplantation may occur during surgical procedures in the abdomen to explain the development of endometrial transplants in scars of abdominal walls.

Summary of Etiology

Although Sampson's theory has received the greatest support it has curiously enough led to a revival of interest in the serosal theory in opposition to his own. But the evidence in favour of any one of the theories is not complete, and therefore one cannot dogmatically support one to the exclusion of the others, a fact which is recognised by even those who have advanced these theories.

Recent Work on the Subject

With the formation of endometriosis there are two factors concerned--- (1) the source of the ectopic endometrium (2) some factor which determines its development. The source is still the subject of controversy, but it is generally agreed that the development of the tissue is related to ovarian function. Groves in 1930 proved in rabbits that the presence of oestrogenic principle is essential for the maintainence of the endometrial transplants. Recent work tends to link up ovarian dysfunction with the condition of endometriosis. All authorities report a high incidence of uterine fibroids and menstrual irregularities in this condition. This suggested to Allen that endometriosis is a manifestation of a cellular metaplasia caused by glandular dysfunction. Jeffcoate and Potter made a clinical and pathological study of 111 cases of endometriosis and demonstrated follicular overactivity in the majority of them. Since excess ovarian follicular hormone has been proven to be the cause of endometrial hyperplasia,—and since the morphological and functional characteristics of aberrent endometrium are similar to uterine endometrium, it seems logical that the factor determining the development of cellular metaplasia or implantation proliferation is the oestrogenic principle. (Witherspoon).

Clinical Features

Greene-Armytage reports an incidence of 8.9% in 1000 consecutive surgical cases. Dougal states the incidence is 10% of all gynecological operations. It occurs only in women.

It occurs usually during the period of menstrual activity although some cases have been reported in women past the menopause; (these have been explained by the fact that glandular activity regresses gradually from the time of the actual cessation of menstruation.)

It has never been found before the menarche, the average age of onset being about 35. (Henderson.)

All authors report relative sterility as a common finding. It is reported in from 20% to 70% of cases.

Physiology and Gross Pathology

Dougal classifies endometriosis as—

1. Interna—in which the lesion is found in the wall of uterus, and is otherwise known as adenomyoma of the uterus. Henderson draws attention to the fact that it resembles other forms histologically but rarely do the two conditions occur together.

2. Externa—which includes lesions of the ovary, pouch of Douglas, recto-vaginal space, external surface of the uterus, bladder, rectum sigmoid, inguinal canal and umbilicus.

ADENOMYOMA OF UTERUS

The lesion consists of a diffuse or nodular thickening in the muscle wall and is most frequently found near the cornu. It grows slowly and is not encapsulated, thus being distinguished from fibroma. It is composed of an area of hyperplastic fibromuscular tissue interlaced by seams of endometrium. The surface mucosa is not increased in thickness. This invading endometrium may in spots become pinched off and form gland-like spaces, which may be converted into haemorrhagic cysts by menstrual reaction of the wall.

ENDOMETRIOSIS OF THE OVARY

This condition is manifested in one of three ways:

1. The ovary appears normal but is adherent to the broad ligament or to the pelvic floor. This is due to endometrial tissue on the surface of the ovary which often invades it, without the formation of endometrial cysts or hematomas. Often the lesion may be diagnosed only on microscopic examination.

2. The presence of cysts which are wholly or partly lined by tissue with the histological structure of mullerian mucosa. Early ovarian lesions are found on the lateral and under surfaces of the ovary, nearest to the opening of the tube. Those on the surface are usually small, 2 to 4 cm. in diameter, and frequently bilateral. This represents a later stage than type 1 in which a menstrual reaction has occurred in the wall with the escape of blood into the cavity. These cysts tend to perforate early but promptly seal over again. The ovary becomes adherent to adjacent structures at the point of rupture. The cysts found deep in the substance of the ovary attain a larger size, up to 9 cm., because they do not perforate as readily. There may be repeated perforation if there is repeated filling with blood but the ultimate tendency is retrogression since the epithelium is destroyed more rapidly than it is replaced.

3. There may be hematomas in which mullerian tissue lining is lacking. These may be classed as endometriosis if they are adherent to other structures, if endometriosis is present in adjacent structures or if there is evidence of previous rupture.

Ovarian endometrial cysts should not be confused with either cyst adenomas of the ovary with haemorrhagic contents, or ovarian hematomas of corpus lutein origin. They may be differentiated from other ovarian cysts by the fact that they characteristically show perforation with a raw area of ovarian tissue about it. Also their walls are thicker and do not tend to collapse as retention cysts do. The lining may be rough and brown due to old haemorrhage, or it may be smooth and gray.

ENDOMETRIOSIS OF THE PERITONEUM

The lesions are characterized by the well-known results and peritoneal irritation such as granulation and scar tissue, adhesions and various peritoneal inclusions. And also by the presence of endometrial tissue either on the sur-

face of, or embedded in the lesions. The earliest lesions consist of purplish blue cysts which vary in size from a pin head to 1 cm. in diameter. They may occur singly but usually are in groups scattered over the pelvic peritoneum, most often on the back of the broad ligament under cover of the ovary. Later on stellate scar-like areas may be seen which represent areas which have healed after destruction of the contained epithelium. Occasionally clear, firm cysts are present and more rarely the whole peritoneum may present a pig-skin appearance. Endometrial implants are most common where the peritoneum is folded irregularly as at the outer border of the sigmoid, at the attachment of the epiploic appendices and in the pouch of Douglas. In occasional cases all the organs in the pelvis, including the rectum and sigmoid, are matted together. The growth occasionally encircles the ureters.

ENDOMETRIOSIS OF THE RECTO VAGINAL SEPTUM

This condition may be co-existent with peritoneal and ovarian endometriosis or may exist as a primary intraperitoneal lesion. The growths vary from the size of a pea to large masses obliterating the pouch of Douglas. They may be discrete but often appear to grow from the back of the supravaginal cervix, spreading out along the utero-sacral folds and broad ligament to the rectum.

ENDOMETRIOSIS OF THE RECTUM AND SIGMOID

This is one of the rarer consequences of pelvic and recto-vaginal endometriosis. From the peritoneal surface the lesion produces a puckering of the serosa, and scarring almost identical with that produced by carcinoma. But it differs from carcinoma in that it does not tend to encircle the bowel, it does not invade the mucous membrane which can be visualized intact from the lumen of the gut, and the lymphatic drainage is not involved.

PRIMARY FIMBRIAL ENDOMETRIOSIS

Sampson in 1932 described a condition of primary endometriosis of the tubal fimbriae. By histological study of such cases he believes that they arise in the terminal part of the mucosa of the tube at or near the mucoserosal junction. This growth, if occurring in ovarian fimbriae, may give rise to ovarian endometriosis.

MICROSCOPIC PATHOLOGY

The picture in all the lesions is fairly uniform and consists of epithelium, stroma and muscle tissue. The tumor masses are not encapsulated. There are gland spaces scattered throughout. They vary in size, and may be empty or filled with dark blood and cellular detritus, depending on the stage of the menstrual cycle. These spaces are lined by a single layer of low cuboidal or cylindrical epithelium with deeply staining centrally placed nuclei. In many cases the cells are ciliated.

The stroma typically consists of loosely packed fibrous tissue and round cells. Non-striated muscle fibres are also found scattered throughout. The stroma may be absent, and the epithelium is then low cuboidal. At the menstrual period the epithelium may be lifted up from the stroma by haemorrhage, there may then be rupture through the overlying epithelium.

Symptomatology.

The importance of the disease lies in the fact that the lesions are of a diffuse and infiltrative nature, which though not histologically malignant, may simulate carcinoma. The underlying cause of the symptoms is due to the fact that the lesions react to menstruation.

It is agreed that the most outstanding symptom is acquired dysmenorrhoea. The amount of pain which the patient experiences depends on the site and effect of the lesion rather than its size. The pain usually comes on a few hours or days before the

menstrual flow and continues through it, or may cease when the flow is established. In come cases it comes on a few days after the period, or it may be a continuous pain with exacerbations at the period. Contrary to the pain of inflammatory origin, this is made worse by the application of heat. The pain is usually dull and aching in character but may be sharp and stabbing. There may be acute recurring attacks of pain simulating appendicitis, due to rupture of a cyst with the escape of its irritating contents. The situation of the pain gives some lead as to the site of the lesion. It is usually in the lower abdomen, either right or left quadrant. Pain over the sacrum is caused by involvement of the pouch of Douglas. Rectal pain occurs in cases involving the recto-vaginal septum, the rectum or sigmoid. Dysuria with the menstrual periods may signify involvement of the bladder or ureters.

Menorrhagia is another common symptom present in about one-half the cases but in the majority of these fibroma are also present, which could explain the symptom. It is believed to be due mainly to disturbed ovarian function.

Dyspareunia is another complaint, occurring in cases with rectovaginal involvement.

Nausea and vomiting may be accompaniments of the menstrual period, but King reported intermenstrual vomiting not related to food, in one quarter of his cases.

Diagnosis cannot be made on isolated symptoms alone but rather on a symptom complex as set forth by Keene and Kimbrough.

1. Age—25 to menopause.
2. Sterility—absolute or relative.
3. Abnormal menstruation—usually menorrhagia.
4. Acquired dysmenorrhoea.
5. Sacral backache.
6. Dyspareunia.
7. Intermittent lower abdominal pain increased at menstrual periods.
8. Pain in rectum or bladder with distinct relation to menstruation.

Physical Findings.

In the majority of cases these are not typical.

1. *Adenomyoma of Uterus.*—Usually this cannot be differentiated from myoma but there may be tenderness out of proportion to size.

2. *Ovarian Endometriosis with Well Developed Peritoneal Implants.* — The signs are based on the fact that adhesions have caused a relative immobility of pelvic organs which causes pain on an attempt to change the position of the uterus. On one or both sides of the uterus, and blending into it is a tender, densely adherent semi-solid or firm mass. The uterus is retroverted in many cases.

3. *Rectovaginal Endometriosis.*—This gives typical physical signs of a tender retrocervical thickening which may be nodular or ridge-like. On vaginal examination cysts may be seen bulging into the vault. If the growth involves the rectum it may be seen or felt as a mass on the anterior wall. It is differentiated from carcinoma by intact mucosa.

4. *Endometriosis of Umbilicus or Groin.*—This is characterized by a tumor which swells at menstrual periods. Bloody discharge from the umbilicus without previous abdominal operation is pathognomonic of the disease but if there has been a previous operation it may be caused by a true fistula leading to the uterus.

5. *Involvement of the Bladder.*—Cystoscopic examination reveals typical bluish cysts covered by the mucous membrane of bladder.

Treatment.

Activation and proliferation of the lesions depend on the presence of ovarian function and a progressive atrophy of the lesions follows removal of the ovaries. It is a difficult problem, however, since the disease occurs most often among young women. It is gen-

erally agreed that surgical treatment is the method of choice but in some cases X-ray of ovaries may be used to produce an artificial menopause. Radiation of the growth itself has no effect.

Conservative treatment is used, if possible, in the cases of smaller ovarian adenomas and rectovaginal growths. These may be cauterized or excised, leaving some ovarian tissue to function. In some cases this may be undertaken with the understanding that more radical treatment will be necessary at a later date. No treatment is necessary for peritoneal implants if they are small.

Radical treatment unfortunately is too often necessary. It is used in cases of large ovarian involvement and extensive invasion of the rectum and bladder. It consists in a bi-lateral salpingo-oophorectomy and hysterectomy but does not require excision of the other affected areas, as these gradually regress over a period of months.

Conservative treatment results in a cure of about 70% of cases, while radical treatment is 95% to 100% successful. (Keene and Kimbrough).

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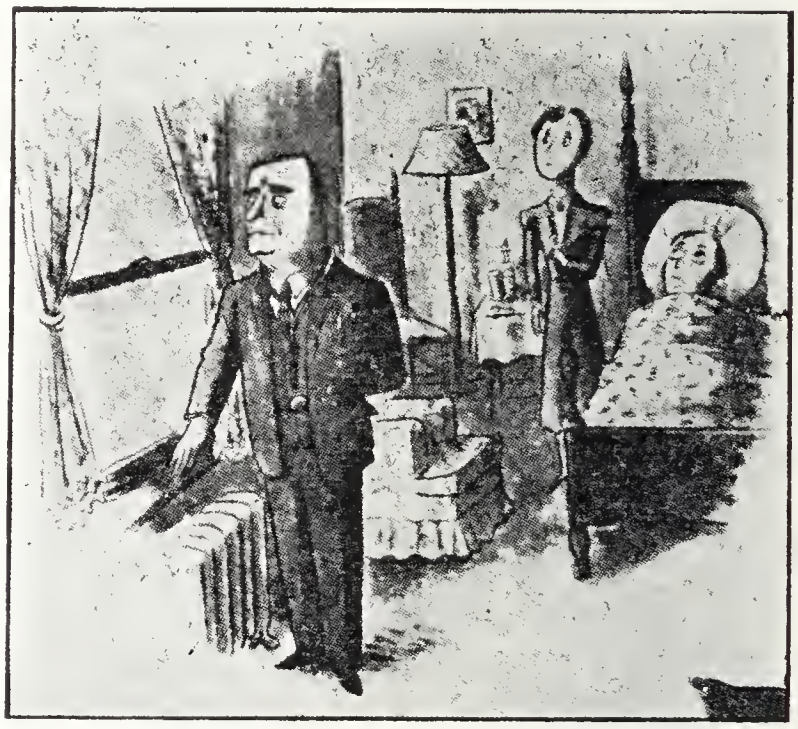

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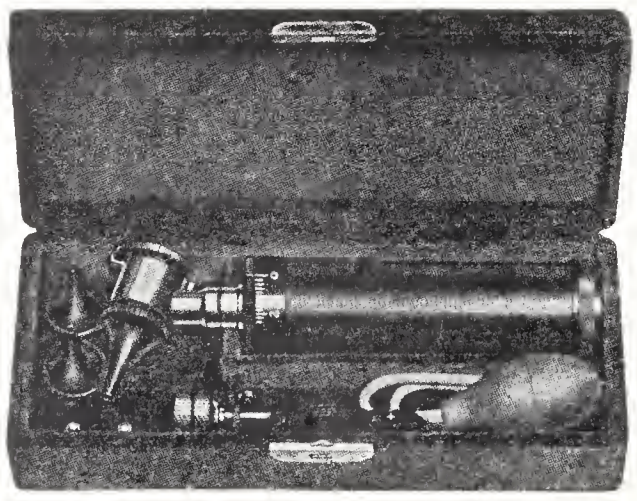

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THE TREATMENT OF DIABETES MELLITUS

By M. P. HOOVER, '40.

Diabetes mellitus is a disease characterized by an increase of sugar in the blood and excretion in the urine, dependent on disease of the pancreas, especially the islets, which are functionally related with other endocrine glands and the liver. Insulin not only promotes normal accumulation of glycogen in the liver, muscles and skin and combustion of glucose in the tissues but also exerts a control upon protein and fat metabolism. Another shorter but less explanatory definition is that diabetes is a disturbance of carbohydrate metabolism in which the normal balance of the regulating factors is lost.

From the above statements it is evident that diabetes mellitus is a disease in which the underlying physiological disturbances are quite complex. It has been found that the pancreas and its activities are associated closely-with the pituitary, thyroid, adrenals, and gonads as well as the liver, muscle and skin tissues. Thus the problem of discovering the inter-relationships of the various factors at fault is obvious.

Before starting to treat any condition it is well to appreciate the cause, if that be possible, because the ideal form of treatment is that which, having determined the cause, proceeds to eliminate it with the consequence that the disease is at least arrested, if not completely cured. Also by knowing the cause we can then adopt measures to prevent the occurrence of the condition; this is the ultimate goal of medical practise. What do we know of the cause of diabetes mellitus? It must be admitted that the real cause is not known. However, certain predisposing factors are associated with the disease:

1. *Heredity*—The view has been presented that certain individuals, contain an "individual inherited disposition" with its seat in the nervous system. Various observers have noted the tendency for diabetes to run in families.

2. *Diet*—The opinion has recurred repeatedly that over-indulgence in food especially of carbohydrate is a causative factor. The association of obesity and diabetes has long been known; it is now believed that overindulgence in food helps to provoke the condition but only in a predisposed person.

3. *Race*—It is more prevalent among Jews than any other race.

4. *Nervous Factors*—Severe nervous and psychical shocks are definitely known to provoke the disease. Injuries and diseases of the central nervous system are sometimes responsible.

5. *Infections* — Various infections may aggravate a diabetes or institute a very mild form, which, however, is only temporary. There is no evidence to show that an infectious agent is really at work.

It is now seen that the true cause of the disease is not known. Data seems to point to the conclusion that it is usually associated with a constitutional tendency or weakness and the only way that this can be altered is by selective breeding. To this end it has been suggested that two diabetics who marry should not have children, and that two individuals from diabetic families should be discouraged from having children. Since the exact place of heredity is not known, no one can be dogmatic on this question. Intelligent regulation of the diet to prevent obesity and maintain general good health, elimination of foci of infection, nervous tension and depressive mental states are suggested as habits worthy of being considered in the interests of prevention. From the nature of the condition and the obscurity of the etiology, the conclusion is evident that

treatment must deal primarily with the upset physiological processes; it must readjust the abnormal metabolism, treat symptoms if necessary and deal with complications as they arise. At present, cure is impossible, so that treatment must be continued throughout life.

As a rule, treatment is advised in hospital; here the patient usually does better because he learns the routine of treatment more quickly and is freed from the minor worries and responsibilities of home life. The education of the patient is the very foundation for its success because the management of diet, insulin administration and personal hygiene must be continued indefinitely. However, office treatment can proceed if the case is not too severe and the doctor has adequate time to devote to it. It is an axiom that no patient can travel alone even though his condition is apparently controlled. Careful supervision by means of a regular follow-up service is essential and the doctor must always be on the outlook for upsets, complications and deviations from health and if these arise, prompt treatment must be instituted. The patient is instructed right from the start how to do a Benedict test for sugar and also a ferric chloride test for acetone bodies; these are done every day at home and enable him to watch the progress and effectiveness of the treatment. At every visit to the office the doctor does a urinalysis, blood sugar determination and physical examination, not only to inform him how he is progressing but to keep him interested. It is most important that a cheerful outlook be created in such a patient because discouragement and lack of interest are not conducive to continued perseverance in the treatment.

Diet.

There is no unanimity regarding the best type of diet but recent leanings are toward a more liberal amount of carbohydrate. The basis of the dietary treatment is to supply enough protein, fat and corbohydrate when the diabetes is under control and yet not aggravate the condition. The diet should be so simple that it is easily learned; it should provide essentials for physical health and not be monotonous or unduly limited in variety. Except in the very severe case, and fortunately the majority are mild, the dietary restriction should not be severe; this is much different from the older form of treatment where the carbohydrate and protein were severely restricted and the fat high, thus favouring acidosis and coma. A diabetic should never be overfed, and if on moderate feeding the glycosuria does not clear up, insulin is indicated. It is well to realize that a diabetic, like any other individual, lives not on the food supplied but on the food burnt. This is very important at the beginning where the tendency is to restrict the intake unduly; a reduction to 20 calories per kg. per day is allowable for a few days but only for a few. The caloric requirements vary with age, sex, height, weight, surface area, activity and state of nutrition. The most accurate way is to determine the body area from a table and then calculate the requirements for the individual with certain activity. However, the most practical method is to observe the weight over a period of time, sufficient to determine the requirements for constant weight. It is recommended to maintain the body weight slightly below the average. For rapid calculation one may assume that at bed rest 25, light work 30, heavy work 35 calories per kilogram are needed.

In the mild case one starts with the diet that is surmised to be the ultimate one of choice or else a somewhat smaller amount of carbohydrate with very moderate portions of fat and protein and then gradually increase daily the amount given until the required standard is reached; this is determined by maintenance of desired weight, freedom from abnormal fatigue, feeling

of well-being and other evidences of control. Weighing the diet at the beginning has its advantages because it teaches the patient to know the value of foods and prevents over-ingestion. It is foolish to compute values too accurately for the values of foods vary tremendously; indeed it is only necessary to weigh a few foods at first until an idea of value is obtained and then an honest approximation is sufficiently accurate to be satisfactory. The most important point to realize is the relative value of foods and the greater error in over-eating in some than others. For example, four portions of 5% vegetables contain 20 gms. of carbohydrate, while one slice of bread weighing 20 gms. contains 18 gms. carbohydrate. Therefore it is much less dangerous to overeat of vegetables than bread. It is well for the patient to learn the size of an orange weighing 100 or 150 gms. and how much of other fruit is required to supply an equivalent amount of carbohydrate. It is also better to weigh the cereal at first but only for a few times, since a person usually uses the same cereal and the same dish. Potatoes are difficult to approximate; one the size of an egg weighs 60 gms. and contains 12 gms. corbohydrate and 2 gms. protein. The average banana weighs 100 gms. and contains 20 gms. carbohydrate or the equivalent of one slice of bread. Ice cream of 50 or 75 gms. is equivalent to an orange of 100 or 150 gms. These are just a few examples of the way that appreciation of food values may be simplified, resulting in less trouble to the patient. It is usually of great aid to both physician and patient if proper food tables are supplied which point out the composition and relative values of various foods.

There is no common conclusion regarding the amounts of carbohydrate and fat needed. Certain cases which had high doses of insulin but yet had glycosuria were helped by a reduction in fat and an increase in carbohydrate. It has been shown that with a high carbohydrate diet the amount of insulin required to utilize a certain number of grams of glucose is reduced and this tolerance is increased. It is suggested from the above data that it is desirable to include sufficient carbohydrate to give the maximum number of gms. of glucose per unit of insulin without increasing the insulin requirement unduly. Carbohydrate also tends to make the diet more palatable. On the average, 150 gms. are allowed per day.

Sufficient protein must at least be supplied to maintain nitrogen equilibrium. It has been noted that the insulin requirement is lower when the protein intake is low but this is of little practical significance. For young children 2-3 gms., young adults 1.5 gms. and elderly people one gm. or less per kg. of body weight is the average requirement. One egg for breakfast and a moderate serving of meat at noon and night supplies about 120 gms. for the day, and this is usually quite ample. The amount of fat required depends on the need to gain or lose weight and on the calories required to maintain weight and strength. When the case is mild and carbohydrate easily utilized, the fat needed is naturally low. Although the amount rarely goes above the CHO and never above the protein, a dangerous ketogenic anti-ketogenic ration is not to be feared. The usual amount is 85 to 100 gms. per day.

Insulin.

It is better to start all patients on insulin at first as well as putting them on a restricted diet. This procedure saves much time and money and later on when the adjustment has taken place, the insulin may not be needed. Regular insulin (RI) has to a large extent been supplanted by protamine insulin (PI). This is due to the fact that PI has slower absorption and lasts over the much longer period of 24 hours as compared with 6-10 hours of RI.

Protamine Insulin—With the advent of this form of insulin, the treatment

of diabetes has been advanced considerably. It is much simpler to use, requiring only one injection per day, as compared with 2-4 for RI, has abolished many of the reactions obtained formerly and created a more eager and interested attitude on the part of the patient. It is the method of choice in all hitherto untreated diabetics. One starts by giving 10 units before breakfast and then increasing this amount every day or every other day until sufficient is being given to control the condition, as determined by the blood, urine and sense of well being. Usually there is a definite effect in 24 hours although it may not show up for four or five days. One must be careful to realise that if the glycosuria is decreasing, further administration should be discontinued temporarily because a reaction may ensue; also the glycosuria must be decreasing before more carbohydrate is added. If the PI has reduced the blood sugar to normal but yet considerable glycosuria persists, especially in the late afternoon, more PI cannot be given but a dose of RI may be added before breakfast. Usually start the RI with 10 units and vary if needed. Since PI acts more slowly and longer, certain added dietary manoeuvres must be used. The meals are spread farther apart, breakfast earlier and dinner later; certain portions such as an apple or orange, usually taken with a meal should be transferred to mid-morning and mid-afternoon and especially should something be taken at bedtime, preferably in the slowly absorbable form of cheese, crackers or nuts because the blood sugar tends to sink to the lowest level in the early morning hours. These adjustments are necessary because the PI is using CHO better throughout the whole day and thus the reserve supply is lower. Besides, a single addition of carbohydrate lasts only a short period and frequently administration is necessary, particularly after exercise or if a reaction is expected.

In changing over from RI to PI there should be a preliminary period of three days' observation, preferably in hospital, to see how well the diabetes is controlled and form an idea of future requirements. Especially if the total dosage exceeds 40 units, it is best to give some RI together with the PI at first. Begin the RI equal to the former pre-breakfast dose, and also at the same time give a dose of PI equal to the amount of RI usually given during the rest of the day. No more is given that day. In following the case, it is essential to notice the urinary sugar just before the noon meal and on arising the next morning. The former gives an estimate of the effects of the RI and the latter the effect of the PI. Increase or decrease is made gradually, usually 2-4 units at a time, until all the RI is eliminated if possible; the total combined unity is essentially the same as the previous amount of RI. The change-over does not as a rule take more than 10 days.

Regular Insulin—RI still has its place of usefulness in the emergency treatment needed in severe acidosis and coma. This use is based on its quick absorption and action. It is also useful during operations where the blood sugar needs to be rigidly controlled. In some cases RI may need to be used completely at the beginning of treatment. Start by giving 5 units 20-30 minutes before each meal and increase daily till glycosuria is abolished. If the urine is not free from sugar on arising, then give 15 units before each meal; if still not enough, give 2-4 units on retiring. Of course, as mentioned above, it is a very useful adjunct in cases where PI alone will not do.

In summary, the modern insulin treatment is as follows: In the average mild case as much PI is given before breakfast as is needed to maintain control. In more difficult cases enough PI is given to keep the urine free from sugar from midnight until morning without causing reactions. If this fails to control by day, then give a supplementary dose of RI before break-

fast and if necessary a small dose before the evening meal.

Exercise

Exercise is a potent aid in treatment and should be used even though the patient is in bed; one of the greatest handicaps of treating a person in bed is their failure to get adequate exercise. For this purpose the Buerger board is sometimes used. At first the amount should be quite small and should remain moderate until the glycosuria is abolished. It reduces the need for RI but especially for PI.

Complications

There are many complications which will only be mentioned in this article. The majority develop various degrees of the commoner ones if they live long enough. The important ones are arteriosclerosis, which affects mainly the arteries of the legs, feet, heart and brain, severe acidosis, coma, gangrene of the feet, various infections of the skin and a tendency to tuberculosis. The commonest complication is a man made one, namely hypoglycemia. Since this is quite common throughout treatment it may be well to give a short note about it. It is due to an overdose of insulin, too much exercise or too little food. The condition varies in degree and may be characterized by symptoms of great hunger, weakness, tremor and sweating or by the more serious ones of fright, confusion, amnesia, muscular spasms and narcolepsy. Death rarely results. Reactions usually occur 3-4 hours after a meal preceded by insulin and rarely more than 8 hours after; with no food they may come on within one hour. The blood sugar falls to from 20-90 mgm.%. When the reaction is very severe and the patient is not conscious enough to swallow, fluids by mouth must be avoided due to the danger of aspiration and pneumonia. Then give 0.5 to 1.0 cc of adrenalin subcutaneously; this acts by mobilizing glucose from the glycogen in the liver and when consciousness returns in a few moments, sugar or orange juice may be given to supply the need for glucose. If consciousness does not return, then 20 cc of buffered 50% glucose solution may be given intravenously or 5% glucose given subcutaneously. If a reaction is anticipated, it is wise to give food which is slowly absorbed such as bread, meat, cheese or nuts immediately.

Although the treatment of this widespread and serious disease has been greatly benefited by the introduction of protamine insulin, there is no reason to believe that further beneficial developments will not ensue. In fact, the door for further progress still remains open and even already advances are being directed towards the next room of enlightenment. Since the discovery of PI, various other slowly acting forms of insulin have been presented. Protamine zinc insulin is a still more slowly acting form and lasts from 36-48 hours; it is being used very satisfactorily in some cases. As yet the new crystalline insulin, insulin tannate, histone-insulin or any of the other slowly acting forms have not been sufficiently tried.

MEDICAL MANNERS

The Good-natured Scolding

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ON THE THYROID GLAND

By D. J. BREITHAUPT, '41.

The surgical and medical application of the principles our professors have tried so hard to instill into our highly resistant crania, may become somewhat evident in a consideration of the thyroid gland. (Gr. *thyreos*-shield, plus *eidos*-form).

First, we were exposed to biology. There we may have learned that the thyroid gland is an 'H' shaped structure found in vertebrates, which sits astride the trachea (or did we call it the 'windpipe'?). It did not then occur to us, however, that because the gland was common to vertebrates, the potency of an extract of the gland could be tested by noting its effect on the rate of metamorphosis of tadpoles, or on the metabolic rate of rats and mice.

The powers that be had decreed that we should learn something about embryology. Had we chanced to pay any attention there, it would have become evident that the thyroid gland starts to develop about the fourth week of fetal life, as a midline endodermal diverticulum from the floor of the pharynx, just caudal to the tuberculum impar (which becomes incorporated into the anterior part of the tongue). The stalk proceeds, on the cranial side, through, or caudal to the hyoid, then caudad, anterior to the larynx and trachea. The lower end divides into two lobes, each of which are joined on their lateral aspects by thyroid derivatives of the fourth pharyngeal pouch. The original connection between the floor of the pharynx and the isthmus of the gland, the thyroglossal duct, usually atrophies about the sixth fetal week. The normal remnants of the duct are the foramen caecum (L.*caecum*-blind) at the junction of the anterior two-thirds and posterior third of the tongue, and perhaps the pyramidal lobe of the thyroid gland. We did not then perceive that parts of this thyroglossal duct might persist, and later form a growth or dermoid cyst in the mid line of the neck; deep in the tongue between the genio-glossi; below the hyoid bone; or antero-lateral to the thyroid prominence ('Adam's apple'). Such a cyst may burst spontaneously to form a medium cervical fistula. The lateral thyroid rudiments may also fail to develop in the usual manner, and give rise to thyroid rests in the neck or mediastinum unconnected with the main gland. There is of course the possibility of the gland being entirely missing.

Then we were told to look down that formidable machine, the microscope, at what we were given to understand was thyroid gland. There appeared a collection of large pink masses (barely visible to the naked eye) of variable size and often distorted, surrounded by a row of blue dots they called cuboidal epithelium. It was too remote at that time to visualize the possible changes; the enlargement or hypertrophy of the individual cells because they did not have enough iodine with which to build their product, or the hyperplasia of the cells with almost complete disappearance of the pink staining colloid. These changes may occur in response to stimuli such as cold, fright, or sexual disturbances, and are probably mediated by a hormone liberated from the anterior lobe of the pituitary gland.

The time came for us to absorb some anatomy. Since it was perfectly obvious that we must learn the mechanics of this curious human organism before surgery is possible, some of the relations of the thyroid gland may have penetrated deeply enough to remain longer than the day after the examination. We did remember that the parathyroids were outside the fibrous capsuls of the gland, embedded in the fascial sheath. These parathyroid glands

should be avoided at operation or tetany may ensue, due to a low calcium ion level in the blood. We might have remembered perhaps, how many layers of fascia there were to penetrate before reaching the gland (they always were a maze!); that between the capsuls of the gland and the investing pretracheal fascia lies a plexus of veins as well as branches of the entering arteries; and that the nerves supplying the overlying sterno-hyoid and sterno-thyroid muscles enter them low in the neck. Due to this last fact, some surgeons recommend that if the muscles are to be divided, it be done high, remote from the point of entrance of the nerves. Others divide the muscles at the mid point, with no apparent ill effects.

We knew that 'goitre' was an enlargement of the neck due to the thyroid gland. One day it became evident that some of the symptoms of goitre (which has been defined as a non inflammatory enlargement of the thyroid gland) were due to mechanical interference with adjacent structures. Thus pressure on the trachea, recurrent laryngeal nerve, and oesophagus, may produce dyspnea and perhaps emphysema, hoarseness or aphonia, and dysphagia respectively. Pressure on the adjacent sympathetic ganglia may be responsible for ocular symptoms such as exophthalmos, widening of the palpebral fissure, dilated iris, and the slowness of the upper lid in following the eye when the vision is suddenly directed downwards. Chronic tachycardia may also be due to this stimulation of the sympathetic. Pressure on the carotid sheath may give rise to attacks of giddiness and fainting spells. The great veins draining the head and upper limbs are easily obstructed by an enlarged thyroid gland which is sometimes intrathoracic. Pressure may also affect the upper roots of the brachial plexus.

It was self evident that the gland has an arterial supply, as well as venous and lymphatic drainage. It probably did not enter our heads that some day we would want to know the exact situation of those four arteries entering the extremities of the 'H', their origin, and the sympathetic nerves travelling along the walls of the arteries. For the beneficial effects of preoperative ligaturs of the superior thyroid artery are thought to be due to its effect on the nerves running with the vessel, rather than a very significant diminution of the blood supply to the gland. The points of division of the arteries into their glandular branches, and the relationship of surrounding structures, especially the recurrent nerve already mentioned, are worthy of note. This branch of the Vagus nerve controls the abductors of the vocal cords, and if bilaterally injured, an opening must immediately be made into the trachea to permit the patient to breathe. The lymph drainage to the pharyngeal and pretracheal glands, to the lateral deep cervical glands, and to the thymus gland also prove to be of importance, especially in malignant diseases of the thyroid gland.

We were well aware that the thyroid prominence moves on swallowing, and other structures in the neck move with it. It was not so evident that the isthmus and lateral lobes of the thyroid gland move simultaneously because of their attachment to the cricoid cartilage and crico-thyroid ligament by a dense fibrous band. Should the thyroid gland not move on deglutition due to being adherent to surrounding structures, it is significant of some pathological change, possibly cancer.

While trying to organize the cutaneous nerves of the neck, it did not occur to us that some day we would want to know that the supraclavicular and cutaneous colli nerves can be injected for regional anaesthetic block at the middle of the posterior border of the sterno-mastoid muscle; that the transverse process of the third cervical vertebra is close to the posterior border of this muscle at the junction of its

upper third and lower two-thirds, and that by maneuvering a needle just anterior to this, the cervical plexus itself can be injected. In addition to regional block, local infiltration of the limits of the gland is also employed.

About this time we were demonstrating to ourselves that dried thyroid gland (a powdery substance supplied in a bottle) contained iodine, because after a few procedures, the colorless fluid we poured into the test-tube and shook up, became a pinkish violet. Of course we knew that goitre has something to do with iodine, as it is very rare along the seaboard, and is more prevalent in other districts. However, we did not know that two grams of sodium iodide, given over a period of ten days twice a year, to children from their eleventh to seventeenth year, was a very effective prophylactic against enlargement of the thyroid gland in a district where goitre was mildly endemic. In three thousand cases the only ill effect due to this treatment was the occurrence of a slight iodine rash in 0.4% of cases, which disappeared on cessation of treatment. We would have been even more interested had we known of the preoperative use of Lugol's solution (Iodine 5, Potassium Iodide 10, Water to 100). This is used to temporarily relieve the symptoms of thyrotoxicosis, which are usually alleviated for two to three weeks. After this period the symptoms may return and be even more severe than formerly. We might have paid more attention to the amino acids, had we been aware that thyroxine, the active principle of thyroid gland extracts, has the formula of an amino acid, and that it is one of the very few hormones that can be effectively administered by mouth.

It remained for the department of physiology to describe to us the condition of hypothyroidism; the cases of myxedema and cretinism with their lowered metabolic rate and associated symptoms of increased susceptibility to cold, lowered body temperature, dry skin and slow pulse. (Metabolism is defined as the process of oxidation and reduction within the cells of the body, as a result of which life is maintained and heat generated.) These cases also show a depressed mental activity, and increased subcutaneous deposit of protein which does not pit on pressure (the sign of edema fluid). We were eager to learn that these symptoms could be quite effectively alleviated by the administration of thyroid extract. The extract may also be used to overcome adiposity in cases which have a low metabolic rate, when it is convenient to follow its effect by frequent Basal Metabolic Rate determinations.

Conversely, the effects of hyperthyroidism were described. It is held by some that evidence of hyperthyroidism is the indication for operative interference. Myocarditis, high blood pressure, and nervousness may be the only signs of this state. Of course in severer cases there may be more obvious evidence, such as the eye signs already mentioned, the Basal Metabolic Rate increased by 20% or more over the Du Bois standards, tachycardia and palpitation, hot moist flushed skin and increased circulation rate, and lowered susceptibility to cold.

This has been the accumulation of facts, whereas the important principles our professors instill are undoubtedly, the power of accurate observation coupled with logical reasoning. These, as well as knowledge, are needed to differentiate between the state of health and dysfunction, by means of which we hope to justify our existence.

AN EARLY CASE HISTORY AND AUTOPSY REPORT

By H. BOLLEY, 4T1.

Historical Review

"Of their flesh and their carcass shall ye not touch nor eat, they are unclean to you." This biblical generalization thus summarily dismisses the wealth of pathological knowledge that the ancient Rabbinist must have possessed. For it was their practise to minutely examine the entrails of animals killed for food and to pass on them as fit or unfit for human consumption. It is regrettable that skilled as they were in recognizing lesions, they did not attempt to link up these changes with the symptomatology of disease. The practise of examining cadavers to determine the cause of death was left for the sixteenth century when Antonio Benivieni published in 1507 one of the first known records of his post-mortem studies on cases of gall stones, thrombosis of the mesenteric veins, cases of heart disease and senile gangrene. During the Montreal epidemic of 1535 the earliest autopsy in America was performed on a soldier—"ripped to see what the disease was and to seek means to preserve the rest of the company."

Bianca Capello, the grand duchess of Tuscany died of suspected poisoning in 1588 and a protocol records the case. Scurvy accounted for the deaths of Champlain's sailors in 1605 and an inquisitive surgeon performed the autopsies. Dr. Rossiter was requested by the citizens of Hartford in 1662 to examine the body of a child supposedly bewitched. However, the greatest contribution to a systematic performance of post-mortems is attributable to Morgagni (1767) who published his "Seats and Causes of Diseases as Investigated by Anatomy." A voluminous treatise which was his attempt at a pathologic-anatomic explanation of symptomatology. Bichat, Rokitansky and Virchow, of a much later date are considered the pillars of scientific pathology for they taught that every disease represented an anatomically localized process, a generalization pointed out to them by their post-mortem studies.

Confronted therefore with an autopsy report supplemented by its case history, my attention was aroused when I observed that it was dated 1694. Its historical value I thought would be of interest to some, to others a comparison of to-day's records with those of the past. Were it only for these above facts, this article may have never been submitted. But to add to the significance of this finding it was noted:—

1. That three great names of medical annals were linked with this record. (a) Marcello Malpighi—(1628-1694)—the microscopist who also laid many of the foundations of modern pathology and thoroughly familiarized himself with the phenomena of disease and sought their causes in the post-mortem room.

(b) Giorgio Baglivi—(1668-1706)—the Italian Sydenham—who wrote "To frequent societies, to visit libraries, to own valuable unread books or shine in all the journals does not in the least contribute to the comfort of the sick."

(c) Maria Lancisi—(1655-1720) —the greatest Italian clinician of the Period. An epidemiologist who connected the mosquito with "swamp fevers." Wrote two great volumes on "Sudden Death" and was the first to demonstrate the syphilitic aetiology of Heart Disease and aneurisms.

2. That Malpighi was the cadaver!

3. That formal permission to legalize the autopsy was granted. "The learned man (Malpighi) foresaw that he should end his days by an apoplexy and therefore forebade his friends to open his body until thirty hours after his death for he knew well enough that some who seemed dead on a sudden have revived some hours after."

4. That the report was preceded by an accurate description of the illness which did not fail to take into account the mental symptoms.

5. That there was disagreement among the attending physicians as to the mode of treatment. (A predicament that has not changed much these many years!)

6. That the autopsy was orderly conducted, the report concisely written and the cause of death sought for in the brain.

7. That various pathological findings were co-related to the symptoms in an effort to explain them.

8. That Baglivi and Lancisi the disciples of Malpighi were thoroughly familiar with the normal as well as the pathological.

9. That it is paradoxical that the man who contributed so much to our knowledge of Renal Structure should have ended on the table with a "Museum specimen Kidney."

(For economy of space Lancisi's report has been merged with that of Baglivi's, it being similar in the main. Slight diversions are included in parenthesis. I am indebted to Mr. Glassey, my former headmaster, for the translations from the Latin and to the work of Donley on Baglivi's report.)

The Report

"Marcello Malpighi, a man of moderate disposition, of average health and likewise of ordinary stature was now about 66 years of age. During the lapse of several years of his manhood he had been subject to attacks of vomiting (which did torment him for 20 years) together with bilious stools. After some respite from these acid vomitings, he became troubled with palpitations of the heart, stones in the kidneys and bladder and bloody urine. (During the winter he was oppressed at times with gouty pains and with difficulty in breathing.) After his arrival in Rome all these sufferings, especially palpitations of the heart, kidney stones and stinging night sweats became increasingly painful. On the noon of July 25, 1694, he was striken with apoplexy, the seizure being preceded by fits of anxiety and mental sufferings. To the apoplexy were added paralysis of the whole right side of his body with twisting (distortion) of the mouth and likewise of the right eye.

Immediately we tried several Remedies, among them, bleeding from his left arm. My own method would have been to bleed from the paralytic arm, since the obstructed circulation of the fluids in the affected part is restored in no way more quickly than by opening a vessel in the same, as one may clearly prove by the mechanical principles of resistance and motion: this, however, was not done because of the opposing opinions of consulting physicians. In addition we ordered scarifying cupping glasses to be applied to his shoulder blades, the powder of Cornachini, mustard plaster to the soles of his feet and many spirituous cephalic and other remedies specifically useful in Apoplexies. (Purges, diuretics, antipopletic medicines).

After struggling for 40 days with the gravest of perils, namely irrational talking, fullness in the head and other symptoms he was freed by the use of the aforesaid remedies, from his apoplexy and paralysis. But as evils ever tend to multiply themselves, so this illustrious man suffered much from the foregoing diseases with respect of his memory and his power of reasoning: Nay, more, for on the slightest provocation he was dissolved in tears. (One might see by his melancholy countenance but especially by his want of memory that there was lodged in the brain some melancholy humour.) At intervals he was troubled also with loss of appetite, gastric indigestion, twitchings of the muscles and slight attacks of giddiness. Grievously worn out at length by these and other symptoms, he was seized on November 29, 1694, with another apoplexy, after his usual morning enema. This new attack was preceded by very distressing spells of dizziness which lasted almost eight days and was accompanied by bladder spasm due to an impacted stone. Other

symptoms mentioned before were more severe but more serious than all these was the onslaught of a new apoplexy. As all remedies now proved ineffective, he died four hours after the stroke.

"Sectio Cadaveris."

When the body was opened I observed that the left lung was somewhat dried up and blue especially on its posterior aspect where it was adherent to the back. The heart was enlarged by its own mass especially the walls of the left Ventricle which equalled the width of two fingers. (The heart felt harder and thicker in some places than in others. Yet no Polypus was found in it.) The bile in the gall bladder was decidedly black. The left kidney was in its natural condition. The right on the other hand was half the size, and its pelvis was so dilated that two fingers could be comfortably inserted. On account of this dilatation of the pelvis, it followed perchance, that stone which had grown in the kidney at once passed down into the bladder, and from the bladder hurriedly expelled. A thing that this eminent man told me had happened to him many times during his life. (Stones which he voided without pain). In the urinary bladder a small stone was found which had descended there four days before his last stroke, and its passage aggravated those last spells of dizziness. The rest of the viscera were in very good condition.

When his head was opened we found in the cavity of the right cerebral ventricle about two ounces of black clotted blood. The extravasation had passed out of the arteries and was the cause of his Apoplexy and death. In the left cerebral ventricle there still remained an ounce and a half of a yellowish fluid in which there was a small quantity of little grains of sand. The blood vessels of the brain were everywhere dilated. The dura mater was firmly and abnormally adherent to the skull. (This proves that the conglobated glands in the whole body had thrown into the mass of blood an acid lymph and that the conglomerated glands of the hypochondria—especially those of the liver had thrown into it a melancholy humour. These two sorts of humour were thence carried into the vessels of the brain and had disposed the blood to coagulate there, corroding and breaking the tunicles which served for a stop to them and they had run into the cavities where they caused death without a remedy.)

These things I observed when dissecting his body on the

Kalends of December, 1694."

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ACUTE ANAPHYLACTIC SHOCK

By HILLIARD H. VARTY, 4T1.

History.

The detailed study of this curious reaction dates from the beginning of the present century, although observations are on record in the earlier literature which are undoubtedly examples of anaphylaxis. Richet and co-workers (1902) first drew attention to the experimental facts, but the issue was at this time obscured by the chance that the agent selected for study was itself toxic for the particular animal used. Richet observed that dogs which survived a single injection of certain actinians might succumb rapidly, and with a characteristic symptom-complex to a second injection of the same material, given after a period of days or weeks. This substitution of increased susceptibility for the increased resistance which usually follows injections of sublethal doses of toxic material led him to coin the word Anaphylaxis (ana—against, phylaxis—protection). Theobald Smith at about the same time had noted the abnormal sensitiveness of guinea pigs to widely-spaced injections of toxin-antitoxin mixture. Otto (1905) showed that the essential agent in the mixture was the horse-serum, not the toxin; that an interval of ten days elapsed before hypersensitive conditions were established; and that no hypersensitiveness resulted when large doses were given at short intervals. Rosenow and Anderson (1907) showed the specifity of the reaction, that is guinea pigs sensitized to horse-serum were not hypersensitive to subsequent injections of serum of other animals, nor to other proteins, e.g., egg albumin.

Definition.

Not all sudden attacks of dyspnea and convulsions in guinea pigs or of cardiac syncope and cutaneous irritation in man, are manifestations of anaphylaxis. The term should be limited to the typical reaction occurring when a small amount of an otherwise harmless protein is injected into an animal previously prepared at a sufficiently great interval, by injection of the same protein. The following criteria should be met: 1. The observed toxicity must depend on the sensitization of the animals, i.e., the substance must not produce symptoms in non-sensitized animals. 2. Symptoms must be the same as the typical reaction produced in the same animal by injection of other soluble proteins. 3. It should be possible to demonstrate passive sensitization with serum of the sensitized animal. 4. In the case of the guinea pig it should be possible to demonstrate the typical reactions in the virgin guinea pig uterine strip. 5. It should be possible to ameliorate or prevent the bronchial spasm in guinea pigs by proper use of atrophine and epinephrin.

Symptomatology.

Lesions and symptoms are constant for a given species of animal, irrespective of the nature of the sensitizing antigen, but vary sharply from one species to another. The differences as observed in the three species most widely used in experimentation are, in brief:

(a) *Guinea pig*—Animal becomes restless, rapidly goes into tonic and clonic convulsions, respiration slows; becoming violent on inspiration, and ceasing entirely within a few minutes. Death is due to suffocation caused by marked constriction of the bronchioles. Postmortem findings are marked distention of the lungs. This is not prevented by section of the vagi nerves, or by administration of curare and must therefore be of muscular or immediately neuro-muscular origin.

(b) *Rabbit*—Preliminary signs of irritation and violent inspiratory efforts are absent, the animal giving a series of convulsive movements and

dying within a few minutes. Death is due to spasmodic contraction of the branches of the pulmonary artert, followed by the rapid dilation of the right side of the heart, and acute heart failure.

(c) *Dog*—Animal becomes restless, respirations are slow and laboured, and soon shows signs of acute collapse, indicated by extreme fall in blood pressure. This is not due to failure in the output of the heart, or to any influence of the central nervous system, but the collection and stagnation of the blood somewhere in the tissues. For a long time the liver was believed to be the chief site, but it has been shown since that the same reaction occurs in a dog from which the liver has been removed.

Mechanism of Production

It is clear that anaphylaxis belongs to the category of specific antigen — antibody reactions. The only question is the mechanism by which this primary reaction produces the series of events that characterize acute shock in any given species. Two views have been put forward, but these cannot be entirely separated.

(a) *Humoral theory*—According to this theory there is formed in the circulating blood, as a result of an antigen antibody reaction, a toxic substance, anaphylatoxin, which acting on susceptible cells gives rise to the characteristic syndrome. It was soon shown that sera could be rendered toxic by procedures in which there was no antigen antibody reaction. Moreover it is difficult to conceive the formation of an antigen antibody compound, the adsorption of it by a stabilizing serum-constituent, and the consequent digestion of the serum proteins, all occurring within a few moments. Summarizing the work up to this point it is possible to say that sera may be rendered toxic in various ways in the sense that they produce when injected into animals, a syndrome closely resembling, but not identical with, that of acute shock. There is no evidence for the production of an anaphylatoxin, as the result of an antigen-antibody reaction, nor has any mechanism for the production of such been suggested that is compatible with all the known facts. We cannot regard the "in vivo" reactions as denoting an identity of underlying mechanism, although it is highly probable that there is some common factor present in them all. This appears to be the distribution of the histamine sensitive cells.

Cellular Hypothesis—The essence of this is that, for the production of anaphylaxis, the primary antigen—antibody reaction occurs, not in the blood stream, or tissue fluids, but in or on the tissue cells. Early experiments showed that a high concentration of circulating antibodies did not lead to shock. This strongly suggests that "fixed antibody" i.e. antibody which has been removed from the blood and in some way fixed to the cells themselves, is concerned in the reaction. Of great importance were the experiments of Dale, who obtained typical contractions, using the horn of a guinea pig uterus, adding the specific antigen to the sensitized horn. The reaction was sharply specific and after a single maximal response the uterine strip no longer responded, to fresh antigen, showing specific desensitization. Thus the essential features can be demonstrated outside the body.

The role of Histamine—This appears to play an impotrant part. If we regard an antigen-antibody reaction occurring in the cells as the whole story, it is difficult to explain the fact that those tissues playing the most dramatic part in the reaction are exactly those sensitive to histamine, and it is hard to believe that these cells are alone concerned in the fixation of antibody. Cellular injury, however produced, tends to liberate histamine into the tissues. The extent of the histamine effect depends on the amount liberated and on the form in which it is liberated.

Summary

It seems best then to regard acute anaphylactic shock as consisting of two different but related effects — (a) Cell

injury—determined by an antigen-antibody reaction on or in those cells by which antibody has been fixed. (b) Histamine effect—determined by the response of the histamine-sensitive cells. At this time an histological disentanglement of the two reactions is not possible. Whether those cells that are injured and liberate histamine are themselves histamine-sensitive, whether minimal cell injury disturbs the internal economy of the cell so that it becomes sensitive to its own histamine, or whether the injury and liberation of histamine is confined to one type of cell, the response to the liberated histamine to another, are problems as yet unsolved. The different effects is apparently due to different distribution of histamine-sensitive cells.

As regards the anaphylactoid reactions, they differ from true anaphylaxis in that cell injury is not determined by an antigen-antibody reaction; they resemble it in that the secondary histamine effect is the same.

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The writer wishes to express his appreciation to Dr. E. T. Waters for his valuable assistance in preparing this article.

MEDICAL MANNERS

The Stock-in-Trade Joke

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Feature Section

J. C. McCULLOCH, EDITOR

TRAVEL BY CATTLE BOAT

By AL. LANE, '4T0.

Each Spring a number of Medical students suffer from quite a yen to get out and see the world. Whether this is due to the proximity of exams. or to heart trouble is sometimes hard to say. At any rate in the grip of such a wanderlust, the writer last spring signed on a freighter transporting Canadian beef to England. In the hope that an account of life on a cattle boat might be helpful to any students with similar ideas or ambitions this account is written.

The story starts in Montreal where one morning towards the end of May two Medical students from Varsity presented themselves to a cattle exporter, complete with overalls, passport, and a desire to see the world. We were told to report at the stockyards next morning at 9.00 A.M. sharp ready to take the cattle train for St. John, N.B. At the stock yards we spent three hours wondering when something was going to happen, and filled in our time by looking at cows. Previously I had classified all cows as either having horns or not having horns. A new class had to be created for these animals. Apparently they belonged to a class known as steers, the distinction being as far as I could gather that these had once had horns but had had them removed. Later on when we had more experience, and shall we say contact with the animals we were very glad of the omission. 479 of these steers were put on the cattle train. 14 cattlemen were piled into the last coach and with much jolting, jarring and mooing we were off. At first we wondered how they picked out which car to stick us in, but we soon found that it was distinguished from the others by the presence of a stove. Apparently these coaches had been used on the passenger runs before the war but had been discarded. I think it must have been a long time before the war that they were used, but that was merely personal opinion.

Along towards the middle of the afternoon a light lunch was tossed in to us. This lunch consisted of 2 doz. loaves of bread, 2 lbs. of butter, 5 lbs. bologna and 2 lbs. cheese. Luckily someone had a jacknife so we did manage to cut the bologna and the bread. The cheese was easy to manage but 3 inch sandwiches offered some difficulty. After a dubious night's sleep and a breakfast on what was left from lunch we arrived at St. John, and here our work began. The cattle were led off the train into their stalls. From here they passed along a narrow sluice-like affair so set up that the cattlemen could stand and tie a noose around each beast as it passed. Meanwhile the animals were inspected, disinfected and tagged. There was nothing to it except when an excited steer would try and climb out of the sluice. Then the more inexperienced of the hands made a wild dive for the fence and perched on top of it. I might say that our group was quite fortunate, in fact unique, in having one farmer in their midst.

The cattle disposed of, we all set off for the ship where we signed on. First of all we signed a paper agreeing to accept wages amounting to two bits a month. Then we signed a paper agreeing not to accept said wages. This was our first experience with the English conscience. Apparently to sign on a ship for no wages at all "just wasn't done."

Our boat was a remarkably trim craft for a freighter, although someone did make some uncomplimentary references to Noah's Ark. He was soon disillusioned, however, when he found that there were, as one person expressed it, 479 steers and one bull, on board. We sailed at midnight and as soon as the boat had a nice comfortable (?) roll all 14 of us were sent down into the hold. Here we were introduced to the most exciting game, a sort of combination of tag, leap frog and blind man's buff, with a few original variations. The hold was practically as black as a picture we once saw of a negro shovelling coal in a dust storm. There were 480 animals wandering around loose, each with a rope trailing from its neck. The idea of the whole thing was to sneak up on a cow, grab hold of the rope, stick it through a hole in a huge plank running along the front of the stall and tie it tightly before the blame beast got wise and started pulling. At first it was easy, but as

cows got scarcer the going began to get tough, very tough. Of all the perverse obstinate animals ever created cattle come up near the top of the list along with women drivers and a few other evils. We would get a row all nicely lined up except for one space, spend half an hour vainly trying to entice the last animal into position and finally give up in disgust. As soon as our backs were turned the beast would placidly wander down to the end of the row and nose in there. After carefully untying all the animals in the row to make room for him, he would toss up his tail and placidly wander back to his original position. About this time we were ready to commit mayhem, or some other word I can't spell. By the time we were finished we had the cows tied so close together that they had to take turns to lie down.

We were soon initiated into our daily routine. At 4.30 the night watchman would come in with a kettle of boiling liquid that someone with a sense of humour once called coffee. "All up boys, all up; time for caw-feee." After gulping down a mug of this questionable fluid, we would scramble into overalls and gloves, tear out into the frosty air and scurry down into the holds as fast as we could. Here we would dip up bucketfuls of water from huge bins set along the alleyway and set the buckets in front of each animal in turn. 40 head of cattle apiece at 4 buckets a head worked out to 160 buckets and a pair of soaked overalls. At 6 we were free to crawl back into bed unless we were so unfortunate as to be on mess duty for the day. At 7.30 we crawled out again for breakfast. After the first one I never could figure out why. During the day the cows would be given their oats, and later hay and more water. We only did a total of around 4 hours work a day — it was the hours that got us.

The food deserves special mention. Breakfast consisted of boiled beef and boiled potatoes with porridge; for dinner there was boiled beef and boiled potatoes with tea; supper consisted of boiled beef and boiled potatoes with tapioca, known on board as fisheyes. Sometimes by way of variety there was stew consisting of boiled beef and boiled potatoes. However it wasn't as bad as it sounds; on Sunday we got rice instead of tapioca. It seems that Maritime Law requires each ship to supply one pound of meat per day per man. Fortunately they never passed a law that required them to eat it.

Some of the boys had a little difficulty with their appetite and took to wandering out on deck at meal time "to watch the seagulls." In fact our national sport on board was "parking birds." Not a few of the chaps enjoyed the proverbial cattle boat fare of six meals a day — three down and three up. All our washing, dishes and any other washing that was done, was carried out in a bucket. Three days out and some bloody fool left all the tinware in the bottom when he tossed the slops overboard. After that those of us that were eating had to use jacknives, fingers or anything else that came to hand. The breadknife was very useful except that it had a tendency to cut your cheek when the ship rolled.

After ten days on the deep it was a great feeling to find ourselves sailing up the Mersey off Liverpool. Once the cattle were unloaded and we had passed the customs and immigration we were free to do as we liked. (I may make a note here that English beer costs about half as much as Canadian.)

I hope that these few remarks will not deter any of the readers who may be contemplating such a trip as this! The picture is not quite so black as it has been painted; and indeed my personal opinion of cattle boats is that everyone should have the experience —— ONCE.

HIPPOCRATES

By R. M. ARCHIBALD.

We have very little first hand information concerning the Father of Medicine. He was born on the Island of Cos, 460 B.C., into a distinguished Asklepiad family, became the most renowned physician of his time and died about 375 B.C.

Though many of the so-called Hippocratic writings undoubtedly were produced by contemporaries and admirers, they give expression to the ideals of Hippocrates and indicate his influence on the ideals of the Greeks. Everywhere there is evident a love of humanity, a zeal for the enrichment of life and service to the community. He advises consultation for difficult cases and deplores sensational forms of treatment. He wrote for the purpose of recording what he himself knew and had the honesty and humility to record his unsuccessful experiments and the wisdom to learn from his failures. The requisites of a good medical student he lists

as, a natural disposition, favorable location for medical study, early tuition, love of labor, and leisure.

The famous Hippocratic oath, whether or not it originated with Hippocrates, accurately represents the Greek spirit of his time. He who takes oath swears by all Gods to revere, love, and if need be, support his teachers and their offspring; to teach his art only to these and to his own children, and to others bound by medical oath: to treat only to benefit the patient: to recommend or give poison to no one: to give no woman a pessary for producing abortion: to live and practice his art with purity; to leave lithotomy for specialists: to keep secret whatever is seen or heard in the life of man which ought not to be spoken of abroad.

While Hippocrates was reared in and practiced in a famous Aesculpian temple he divorced himself with remarkable thoroughness from most of the superstitions of his cult which he regarded and taught others to regard rather as a practical art. His clear common sense refused to entangle experience, the evidence of the senses and the collection of facts with theological or philosophical speculations. He recognized that diseases are only a part of the processes of nature and are not more or less sacred than other processes. He appreciated the great healing power of nature.

In the Hippocratic writings we find that his humoral pathology explained health as a balance and disease as an imbalance between four humors, blood, phlegm, yellow, and black bile (corresponding with the four Greek elements fire, air, earth and water). The use of the terms melancholy (black bile) and biliousness, (too much bile) is interesting evidence of the influence of his humoral theory on present day terminology if not on modern theory.

Medical Society Notes

BILL ORTVED, Secy.-Treas.

The Medical Society has been a busy organization these last few weeks. The main reasons for this activity may be summed up in the words "Medical At-Home" and "Daffydil."

However the immediate worry for the Society and especially for Bill McGill, is the Dance of the Year to be held in the Royal York on January the twenty-sixth. All arrangements have been completed for this gala affair, and it promises to be a really great party.

Daffydil, too, is not far off. Charlie Sheard who is to head this traditional show with the assistance of Bernie Laski and John Rathbun, still has a great deal of work ahead of him before the final curtain falls. However reports gleaned from many sources suggest a show of no mean calibre, with its full share of that "subtle humour" so characteristic of the medical mind.

Another event of note is to take place in Toronto on February the fourth and fifth. This is the 2nd annual convention of the Canadian Association of Medical Students and Internes. Student representatives are expected from all the Medical Schools in Canada as far east as Dalhousie, and as far to the west as Alberta. Much is expected of this convention as regard the Interne appointment question; and many points for the betterment of the general welfare of both students and internes are to be discussed in this short session. Lloyd Hisey and Bill Ortved, both of 4th year, have been appointed the undergraduate representatives to this convention, from Toronto. The various Medical Schools have indicated their whole-hearted support of the association and through the cooperation of all the schools, the strength of the organization lies. The meetings are to be held in Hart House on this first weekend of February.

The results of the Health Survey conducted throughout the faculty in December are practicallly completed.

Although the Survey lacks the accuracy and finish which a more detailed report could obtain, it still has yielded quite an interesting group of facts. As there was much misunderstanding regarding the question of a health service at the cost of twelve dollars per student per year, it was impossible to gauge the feeling of the students accurately on this question. However this is a question which in some form or another will face the students of the university in the not far distant future, and therefore is one worthy of some thought.

Abstracts

D. H. COPP, *Editor*

Contributors: L. J. Lester, W. H. Perry, J. C. Rathbun, C. B. Shier, H. J. Sullivian, J. G. Watt, R. L. MacMillan

ULCERATIVE COLITIS

By E. R. Cullinan—*Brit. Med. Jour. Dec.* 31, 1938.

Definition: A severe inflammation of mucosa and submucosa of colon, usually with superficial ulceration. Practically always begins in recto-sigmoid and then progresses upwards.

Incidence: Occurs in early adult life. Twice as common in women as in men.

Onset—Diarrhoea and passage of blood and mucus. General health is at first good, and most patients do not seek advice until after several weeks of illness.

Symptoms—(1) *General* — loss of strength and weight. During remission there is often a spectacular recovery.

(2) *Fever*—in severe cases. May last for weeks or months.

(3) *Abdom. pain*—colicky and seldom severe. Relieved by bowel movement.

(4) *G.I.*—Flatulence is common. Anorexia, nausea and vomiting in severe attacks.

(5) *Nervous System*—Marked mental symptoms are very common, especially depression and anxiety.

(6) *Diarrhoea*—up to 40 per day.

Stools—Blood and mucus are prominent. Frank pus is an evidence of ulceration.

Blood — Moderate anaemia, becoming marked during relapse. Half the cases have a moderate leukocytosis (12-15,000).

Sigmoidoscopic—Mucus membrane is reddened, granular and bleeds easily. May be only oedematous, or all stages of ulceration. During remissions, may heal and scar.

X-ray—Enema passes through quickly. Complete lack of haustration in affected part of colon. Narrowing seen in severe cases.

Course—Goes on for years with irregular relapses and remissions. Relapse brought on especially by emotional disturbance; also any acute infection or dietary indiscretion. Complications are few. Probably never cured, but they live for many years.

Treatment—purely symptomatic.

1. Rest in bed and warmth during severe phase.
2. Low residue, high vitamin diet.
3. Iron for anaemia.
4. Adsorbents such as kaolin or charcoal when stools are offensive.
5. Saline or .5% tannic acid irrigations.
6. Liquid parafin gives bulk to stool. Continue indefinitely if constipated.
7. Small, repeated transfusions in severe cases.
8. Surgery-ileostomy.

L.J.L.

ULCERATIVE COLITIS: PERSONALITY STUDIES.

By Erich Wittkower—*Brit. Med. Jour. Dec.* 31, 1938.

Forty unselected cases of idiopathic ulcerative colitis were studied. The great majority were found to have definite psychological disturbance preceding the onset of symptoms. The childhood adjustment of many of these patients could be classified in three groups:

(1) shy, timid and sensitive.
(2) excitable, stubborn and argumentative.
(3) polite, respectful and inferior.

As adults, they could again be placed in three parallel groups, i.e.:

(1) obsessional.
(2) hysterical.
(3) schizoids and depressives.

In most cases there is a clear-cut emotional trauma immediately preceding the onset of the illness, e.g., one woman's symptoms began when her lover suddenly

jilted her. Sometimes the mental symptoms have been observed to decrease during the period of increased bodily symptoms.

Conclusion: Ulcerative colitis is a disease of the mentally ill or maladjusted.

W.T.L.

PELVIC ENDOMETRIOSIS.

By D. N. Henderson—*C.M.A.J., Jan.*, 1939, *Vol.* 40, *No.* 1.

This paper summarizes the findings in forty cases of endometriosis at the Toronto General Hospital. The disease occurs most commonly between the ages of 30 and 40; it is associated with relative sterility, and fibroids commonly accompany the disease. The symptoms in order of frequency were: abdominal pain, menstrual upsets, and dysmenorrhea. The abdominal pain is varied but commonly dragging in nature. Menstrual upsets took the form of menorrhagia in 11, metrorrhagia in 4 and a combination of both in 7. The rectum and sigmoid were involved in adhesions in 23 cases. The treatment is surgical and consists of removal of the ovaries in mild cases and in more severe cases the tubes and uterus are also removed.

J.C.R.

SCIATICA.

Brit. Med. Jour., Dec. 17, 1938, *p.* 1245.

(1) *Sciatica and Its Treatment.*—This is the first in a series of three articles in this issue on sciatica. It concerns itself with differential diagnosis and treatment. The word is defined as meaning pain along the course of the sciatic nerve. The symptom is divided into two types, high and low sciatica, the latter being due to lesions around the sciatic notch of the nature of a perineuritis and characterized by an absent Achilles jerk and a tendency to lean to the affected side. On the other hand, the high type is due to lesions in the neighbourhood of the fourth and fifth lumbar intervertebral foramina. Here the Achilles jerk is often unaffected and the lean is to the contralateral side. The differential diagnosis of the etiological factor is then further elaborated. Finally, treatment is discussed, with the emphasis on the conservative method of rest and analgesics. If insufficient, the injection treatment is indicated, with a discussion of the technique.

(2) *Intervertebral disc lesions as a cause of Sciatica.*—The second article of the series concerns itself with a consideration of the entity now known as "ruptured nucleus pulposus." The anatomy, pathology, symptoms and signs are very thoroughly discussed. Much space is given to, and emphasis laid upon, the subject of radiological diagnosis by means of the injection of lipiodol into the spinal canal. The technique is considered fully and several excellent radiographs shown and interpreted. Then the clinical course and operative treatment are outlined. This article is a very valuable and informative discussion on this syndrome about which little will be found in the standard texts.

(3) *Orthopaedic Aspects of Sciatica.*—In the third and final article of the series, consideration is given to those types that are essentially orthopaedic, that is, to those that are due to anatomical variations of the lumbo-sacral complex. Their diagnosis, pathology and treatment are discussed. In conclusion, it might be said that this is the most helpful and informative presentation of this ill-defined symptom that this reviewer has ever seen.

W.H.P.

DISORDERS OF MENSTRUATION.

By Evan Shute—*C.M.A.J., Jan.*, 1939, *Vol.* 40, *No.* 1.

This paper points out the fallacies in endocrine therapy for menstrual upsets and the possibilities of blood oestrin determinations in order to provide a rational basis for treatment. Endocrine menorrhagia is usually due to or associated with an elevated blood oestrin. Similarly oligomenorrhea is associated with decreased blood oestrin. Dysmenorrhea is often associated with normal variations in blood oestrin and therefore many of the accompanying symptoms may be neurotic in origin. To cases where the upset is related to oestrin deficiency, oestrin should be given and those associated with an oestrin excess should be treated with thyroxin, prolans, progestin or wheat germ oil.

J.C.R.

THE INCIDENCE OF ANOVULATORY MENSTRUATION AMONG PATIENTS OF LOW FERTILITY.

By John Rock, M.D., Marshall K. Bartlett, M.D., and Ronald D. Matson, A.B., *Brookline, Mass.—American Journal of Obstetrics and Gynaecology, Jan.*, 1939.

The paper is based upon the results of a series of 392 women complaining of sterility, about whom adequate information was available. 36 of these, or 9.1%, showed evidence of at least occasional anovulatory menstruation; that is, bleeding from a proliferating or a hyperplastic endometrium, rather than true menstruation or bleeding from a secretory endometrium. Such a differentiation can be made by a small curettage. This provides a useful means for determining the occurrence or failure of ovulation. These examinations

may be repeated frequently, without anaesthesia, as an office procedure.

From this series, 4% of sterility patients may be considered habitually anovulatory, because, for at least several months, they exhibit regular menstrual flow which is clinically indistinguishable from normal menstruation, but which comes from a proliferating or hyperplastic endometrium. Also patients who usually flow regularly from a normal secretory endometrium may occasionally flow from a persisting proliferating endometrium.

Sterility patients with a history of menstrual irregularities, even though flowing normally at the time of examination, should arouse suspicion of anovulatory menstruation, because failure of ovulation is more frequent among such patients than among those whose menstrual history is normal.

Anovulation and amenorrhea are commonly coexistent; and anovulation and regular or slightly irregular menstruation are occasionally coexistent. Ovulation seldom occurs in patients who are habitually amenorrheic.

There is a brief review of the literature concerning anovultory menstruation contained in the paper.

C.B.S.

FRACTURES OF HUMERUS.

By Arnold Griswold, H. Goldberg *and* R. Joplin, *Associates—American Journal of Surgery, January,* 1939; *Vol. XLII, Number* 1, *page* 31.

Fractures of the humerus are classified and reduced as follows:

1. Those above the insertion of the Pectoralis Major. These include:

(a) fractures of head and tuberosities, and

(b) fractures of the surgical neck. The upper fragment is usually flexed, rotated and abducted mainly by Supraspinatus, and the lower fragment is drawn anteriorly and medially by Pectoralis Major. It was believed that the proximal fragment was not under our control, but Howard and Eloesser have shown the intact Biceps tendon gives adequate control when tension is parallel to the body.

2. Fractures of the shaft.

(a) Between insertion of Pectoralis and Deltoid. The upper fragment is drawn medially by Pectoralis Major, and distal fragment drawn upwards and outwards by the Deltoid.

(b) Below Deltoid—no typical deformity.

(c) Supracondylar and condylar. Varus deformity occurs in fractures low in shaft because break in bone results in loss of supinating action of the Biceps. The elbow is under the control of the pronators and attempts to put the forearm in even slight supination results only in supination at the site of the fracture and varus deformity. Therefore supracondylar and low shaft are kept in full pronation during and after reduction.

"T" and "Y" fractures at the elbow are reduced by traction with elbow at right angle and forearm pronated, and the surgeon presses bilaterally to bring the condyles together. In case of isolated medial condyle fracture, the manipulation is the same. If the lateral condyle is broken to avoid valgus deformity, fix in full, supination.

Having partially reduced the deformity, the traction cast is applied which completes the reduction just as suspension-traction methods reduce fractures of the femoral shaft. The traction cast is simply a plaster cast with or without padding extending from axilla to knuckles without regard to site of fracture. The elbow must be at a right angle so that with the patient erect the distal fragment is vertical. The forearm is placed in mid-pronation except when full pronation and supination are required as above.

A loop of wire is incorporated in the upper part of the cast. A sling passes through this, and around the neck. The more distal the sling, the greater is the traction.

After-care. Patient remains erect as much as possible. For the first few nights he should sleep in Fowler's position. Circumduction of the shoulder is begun immediately, by the patient leaning forward and allowing the arm to swing in increasingly larger circles.

Results. In 128 consecutive cases (49 of head and neck, 68 of shaft and 11 supracondylar) all healed satisfactorily except one mid-shaft fracture.

Advantages:

(1) Simplicity.
(2) Applicable to all who can assume erect position.
(3) Comfortable.
(4) Good results.

A REACTION TO THE ORAL ADMINISTRATION OF NICOTINIC ACID

By W. H. Sebrell, M.D., *and* R. E. Butler, M.D., *Washington, D.C.—J.A.M.A., Dec.* 17, 1938.

Nicotinic acid in daily doses of 50 mg., given orally, produced transient, unpleasant but harmless reactions in four of six adult women on a diet restricted in the pellagra-preventive factor. The reaction consists of intense flushing of the face and neck, with itching and a sensa-

tion of heat. The sensations lasted ten to twenty minutes. A daily dose of 30 mg. produced a reaction in two of six women. Therefore reactions are to be expected in some persons on continued treatment with nicotinic acid in daily doses of 30 mg. by mouth.

Although the reactions are disagreeable, they persist only a short time and there is no evidence that any harm is done by them. Their occurrence should not be allowed to interfere with the therapeutic use of large doses of nicotinic acid.

J.G.W.

AN ANALYSIS OF THE STANDARD METHODS OF TREATING FRACTURES OF THE FEMUR.

By D. M. Vickers, M.D., F.R.C.S., *Cambridge, New York—American Journal of Surgery, November,* 1938; *Volume XLII, Number* 2, *page* 332.

In order to evaluate the new methods of treatment of fractures of the femur, e.g., the Smith-Petersen nail, it is necessary to have some yard stick of the results obtained with the older, more conservative methods of treatment. With this in mind, Dr. Vickers reviewed 100 consecutive cases of fractures of the femur.

Fractures of the femur are divided according to their cite into three divisions:

(a) Fractures of Shaft—occurring in the younger age group.

(b) Fractures of the neck—occurring in the older age group.

(c) Intertrochanteric Fractures — occurring in the older age group.

According to their site the results were:

Type	Good	Fair	Poor	Died	Unknown	Total
Shaft	25	2	2	4	4	35
Trochanteric	11	8	0	7	2	38
Mid-neck	11	6	2	6	2	27

The "standard" methods of treatment used were:

(a) Whitman's plaster cast consisting of immobilization of the limb in a position of abduction and internal rotation for ten to twelve weeks, followed by wheelchair and crutches, and allowing no full weight bearing until four to six months. This method frequently results in a stiff knee joint.

(b) Traction. This may be accomplished by skin or bone traction. The latter is more efficient and more comfortable. Bone traction may be accomplished by special "ice-tongs" attached to the femoral condyles or by Kirschner wire passed through the condyles above the synovial prolongation of the knee joint. This method allows early movement and hence stiff knee and ankles are avoided. Once the mode of traction has been chosen the limb can be suspended or extended by weights as desired. According to the type of treatment the results were:

	Number Treated.	Recovered.	Died.
Cast	28	28	0
Suspension	13	13	0
Extension	46	39	7
Untreated	13	3	10

Dr. Vickers concluded by emphasizing the good results obtainable by standard methods, if sufficient time is allowed.

H.J.L.

STUDIES ON THE MECHANISM OF THE ACTION OF SULFANILAMIDE.

By John S. Lockwood, M.D., Alvin F. Coburn, M.D., *and* Herbert E. Stokinger, M.D., *New York—J.A.M.A., Dec.* 17, 1938.

This article is a study of the effect of sulfanilamide on the various types of infections as they occur in man. The drug was administered at intervals, chiefly by mouth. Infections treated included those caused by the hemolytic streptococcus, meningococcus, gonococcus, Streptococcus viridans and pneumococcus.

Toxicity of Sulfanilamide: No Relation to the Therapeutic Effect.

Approximately half of the adults and one fifth of the children showed some toxic manifestations. Some of these are mild and others alarming.

(1) *Mild Manifestations*

A. Cyanosis.—The development of cyanosis in patients receiving sulfanilamide therapy was noted in 50 per cent of adults and 20 per cent of children. Most persons became blue before the third day of drug therapy. The intensity of the colour depends on the amount of drug in the circulation rather than the amount administered. This formation of methemoglobin may aggravate diseases that are accompanied by lowered arterial oxygen, such as pneumonia, and cardiac insufficiency.

B. Gastrointestinal Symptoms.—Anorexia, nausea, vomiting, abdominal pain and occasionally severe diarrhoea occur. Infants present an acute problem when the anorexia and vomiting interfere with their nutrition. The symptoms disappear when the drug is discontinued.

C. Disturbances of the Central Nervous System.—Dizziness, headache are common. Mild personality changes, especially lightheadedness and depression, but occasionally maniacal and disorientation symptoms appear.

D. Sulfanilamide Fever.—This is rare in children but common in adults. It is usually a slowly rising fever reaching a peak of 106 F. in some instances. In a few hypersensitive subjects who had been sick following previous administrations, as little as 0.6 Gm. of the drug caused aches, chills, temperature spiking to 104 F., and a leukocytosis as high as 30,000 cells per cu. mm.

E. Precordial and Abdominal Pain.—This occurred mainly in patients who showed other evidence of toxicity to the drug, such as cyanosis.

F. Acidosis.—This is not a frequent sequel, and it clears up rapidly when the drug is discontinued.

(2) *Severe Manifestations*

A. Rash.—A maculopapular rash resembling confluent measles develops in a few cases. The rash persists for two days or after the drug is stopped. Itching is occasionally severe.

B. Jaundice.—There are two types which appear; one due to acute hemolytic jaundice, the other the result of hepatitis.

C. Anemia.—A severe hemolytic anemia, attributable to the drug, develops even after moderate dosage with sulfanilamide. It is progressive anemia, but it can be partly counteracted by transfusions.

D. Hemoglobinuria.—In two cases hemoglobinuria developed shortly after administration of moderate doses of sulfanilamide, and in one of them the hemoglobin level fell alarmingly.

E. Granulocytopenia.—Two cases, both females, had a marked depression of leukocytes, but the infection may have been largely responsible for the granulocytopenia.

(3) *Secondary Reaction: Late Manifestations*

In one man jaundice, pyrexia of 105 F., enlargement of the liver and spleen, and rash developed 18 days after discontinuance of the drug.

The Problem of Relapse Following Withdrawal of Sulfanilamide

Reappearance of Organism Without Symptoms.—In cases of acute pharyngitis and tonsillitis, the hemolytic streptococci appeared in the lesions in almost pure culture, 72 hours after sulfanilamide was withdrawn.

Reappearance of the Organism With Mild Symptoms.—Some patients who show a return of the infectious agent experience mild symptoms but less severe than the original disease.

Recurrence of Severe Disease.—This is similar to the original disease, and postpartum infection sometimes behaves this way.

Development of Metastatic Lesions and Bacteremia

Bacteria remaining in necrotic tissues can become highly invasive after the withdrawal of sulfanilamide, as evidenced by the number of cases of metastatic lesions, or hemolytic streptococcus bacteremia that occurred a few hours or days after the drug was stopped.

The Relation of Free Surgical Drainage to the Effectiveness of Sulfanilamide Therapy

Sulfanilamide seems to be of no therapeutic value against well developed abscesses, but in these cases surgical drainage brought prompt relief. However, the use of sulfanilamide will prevent the formation of metastatic lesions and limit the infection to its original focus.

In necrotic lesions containing both hemolytic streptococci and hemolytic staphylococci, the sulfanilamide was found to be ineffective even with free surgical drainage.

The Effect of Sulfanilamide on Rapidly Spreading Infections

Sulfanilamide is most effective against rapidly spreading infections with little tissue destruction, such as cellulitis, hemolytic streptococcus septicemia, and mastoiditis. In the case of mastoiditis the sulfanilamide prevented further spread of the infection but was unable to kill organisms in necrotic bone.

J.G.W.

CEREBRAL LESIONS IN HYPOGLYCEMIA

By A. B. Baker, M.D., *Minneapolis.—Arch. of Path., Oct.*, 1938.

With the increasing use of artificial hypoglycemia in the treatment of schizophrenia, acne, morphinism and other conditions, the problem of the cerebral changes that might result from such therapy becomes paramount. In the mild cases the lesions are only transitory but in the more severe attacks the lesions may persist for days or become permanent. The more severe lesions may be divided into three groups:

(1) Cerebral petechia.—These vary from small extravasations to large haemorrhages that tear into the brain substance and produce definite cerebral damage.

(2) Large areas of encephalomalacia, demyelinization and cyst formation. These huge areas of softening must result in

functional damage. Cysts are believed to be due to the pressure from fluid accumulating within the cerebral fissures.

(3) Diffuse, generalized glial proliferation and extensive gliosis around the areas of softening.

It is apparent that any single one or any combination of these cerebral alterations is sufficient to produce severe, lasting injury of the brain, permanent functional damage or death. The author, however, does not advise the widespread discontinuance of insulin shock therapy, but recommends conservatism.

J.G.W.

A SURVEY OF THE SO-CALLED HEMOLYTIC ANEMIAS

By O. H. Perry Pepper. M.D., F.A.C.P.—*Ann. of Int. Med., Dec.*, 1938.

This author begins his article by pointing out the lack of clear separation between the various groups of anemias. Hemolytic anemias are those in which hemolysis is the chief but perhaps not the sole factor. Erythrocytes are destroyed in three ways (1) normal wear and tear, (2) reticulo-endothelial system—it does not slaughter healthy cells, (3) hemolysis—no hemoglobin in normal plasma therefore this factor is not believed to be present normally.

A classification of hemolytic anemias is given according to the mechanism of hemolysis.

(1) Fault in erythrocyte
  (a) hemolytic ictero-anemia
  (b) sickle-cell anemia
  (c) hemolytic feature of pernicious anemia.

(2) Parasitic destruction of erythrosytes
  (a) Malaria
  (b) Oroga fever

(3) Allergic hemolysis
  (a) favism—does not follow first eating of bean, only upon subsequent ingestion in sensitized individual
  (b) occasional drug sensitivity, for example—sulphanilamide

(4) Chemical agents
  (a) exogenous-acetanilid, lead, snake venom
  (b) endogenous
    (1) by bile salts—in infants with jaundice?
    (2) altered plasma p.H. — paroxysmal hemoglobinuria due to lowering of p.H.
  (c) conditioned—indol in dogs on deficient diet

(5) Bacterial toxin
  (a) B. Welchii
  (b) unidentified infection as in some cases of acute hemolytic anemia of Lederer

(6) Mechanism unknown and not definitely hemolytic—Cooley's anemia, erythroblastoses of infancy and carcinematosis?

(7) Specific hemolysins—transfusion of incompatiable blood

(8) Physical agents such as cold—paroxysmal hemoglobinuria of tertiary syphilis.

(9) Excessive destruction in reticulo—endothelial system as in reticulo-endotheliosis, Hodgkin's disease

(10) Phagocytosis by leukocytes; phagocytic anemia

Common Features of Hemolytic Anemias

(1) Immediate evidence of increased blood destruction—yellowish facies, urobilinuria, hemoglobinuria

(2) Hyperplasia of reticulo-endothelial system: enlargement of liver and spleen

(3) Regenerative activity of hemopoetic tissue—immature white and red cells

Prognosis and treatment depend on the hemolytic activity, severity of the anemia and the regenerative process. If the hemolysing cause is removed the prognosis is good and in hemolytic ictero-anemia splenectomy reduces the hemolysis although susceptible red cells are still present. Transfusions relieve the severity of the anemia.

Conclusion.—The author states that knowledge, understanding and treatment of hemolytic anemia are in a very unsatisfactory state compared to that in pernicious and deficiency anemias. However, hemolytic anemias possess many features in common and by appreciation of these group behaviours and by an interpretation of these diseases in terms of disturbed physiology i.e. an upset hemolytopoetic balance, a state of clearer understanding should be attained.

R.L.M.

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Book Review

THE LIVING BODY

Best and Taylor. 538 *Pages*. $3.60.

Here is a new volume by the famous Toronto team of physiologists, that will indeed be an aid to all of us. "The Living Body" is patterned after the larger text, familiar to the third year men. This volume is much briefer and yet contains the meat of physiology, without any of the useless fat. The same type and paper, and many of the diagrams of the bigger book are used.

This book is free from long, intricate arguments and wearisome experimental details. One does not find himself on the verge of apoplexy, after he has pored over the pages of Jonestein's views, to find on the following three pages Smithberg's theories to the contrary; and finally, after memorizing formulae and figures in the latter's work, read that much more work is needed before the truth is obtained. As the authors put it — "For the beginner the picture must be drawn with a broad brush, the finer strokes being omitted lest they detract from the boldness of the outline."

Although an average knowledge of physics and chemistry is assumed, there are descriptions of Anatomy and Histology where they are required.

This volume should be useful for the first year man, who may read it on Sunday afternoons, as did Dr. Boyd read Milton. The sophomore could read it while swinging in a hammock, in July. The third year student will find it a good introduction to lectures. It may help senior men in reviewing their physiology. Nurses, dentists, etc., may find it helpful. The layman would be wise to stick to "The Human Body," by the same authors. That our faculty should preserve a scientific uniformity, perhaps a good title for Dr. Grant's excellent volume would be "The Dead Body."

A. M. Vaughan, 4T1.

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